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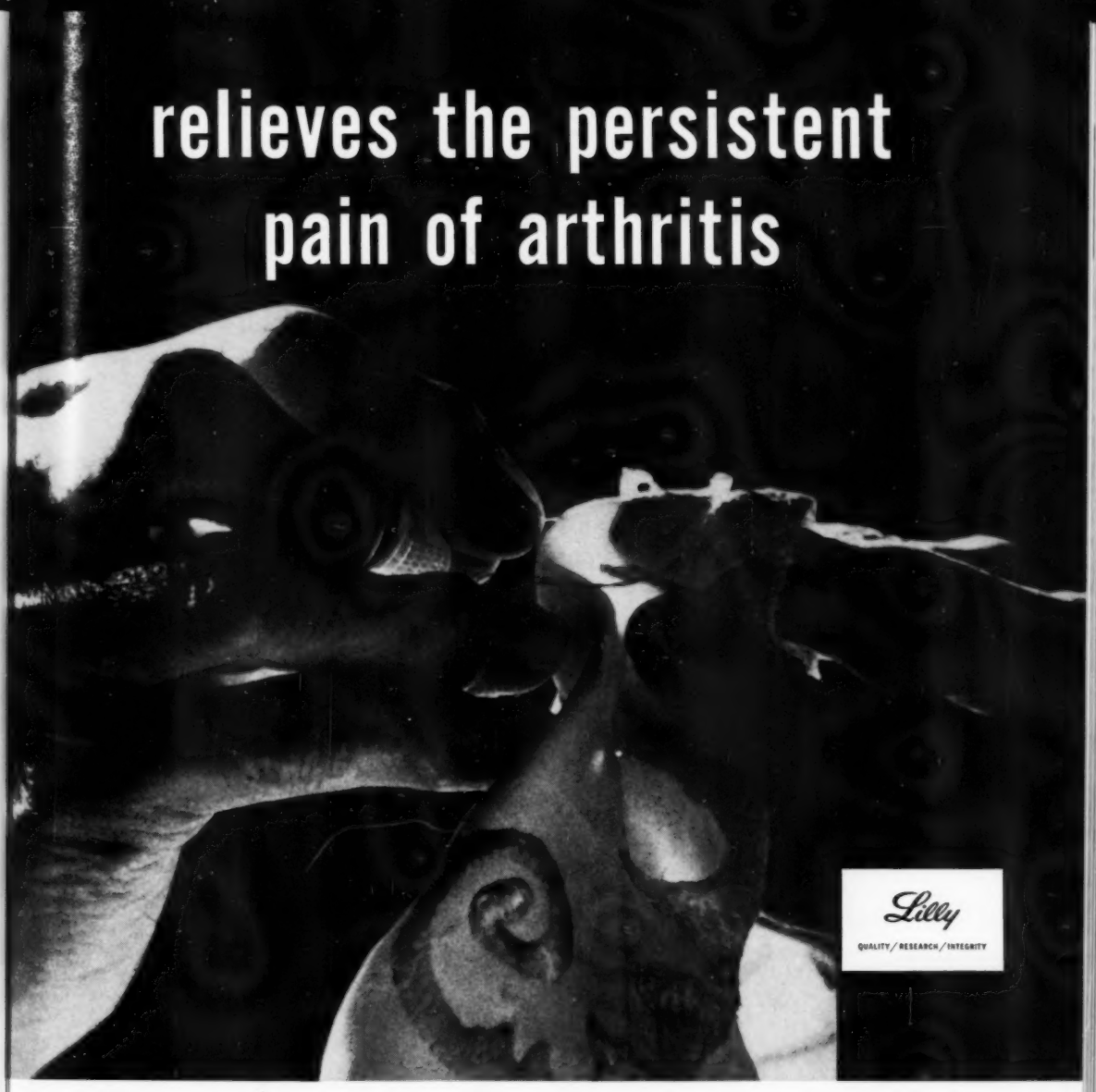

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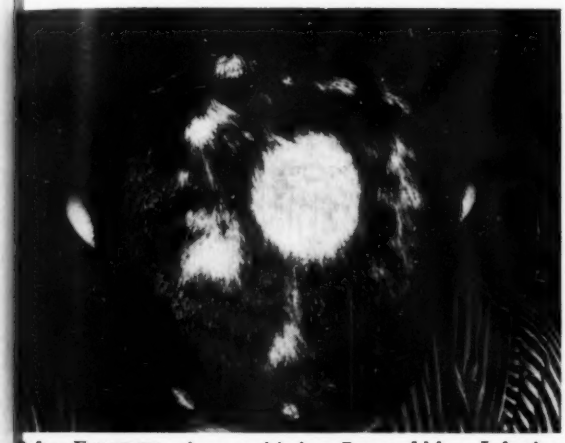
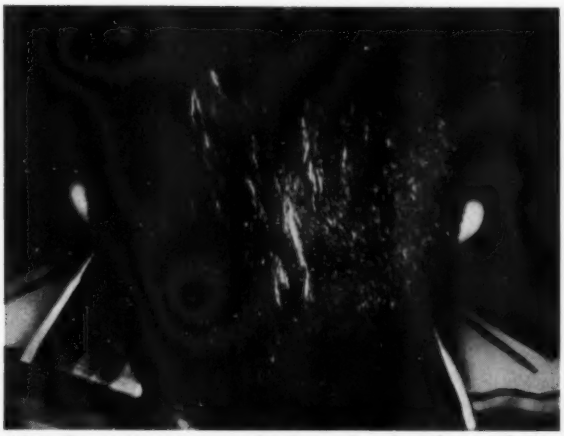


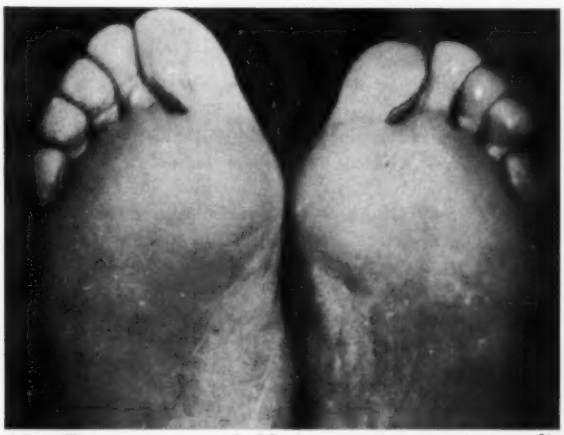
Before FULVICIN—tinea capitis in a 7-year-old boy. Infecting organism: *Microsporum audouini.* Duration of disease: 1 year.



After FULVICIN—tinea capitis 2 months after the conclusion of 6 weeks of oral treatment.

PHOTOS COURTESY OF M. MURRAY NIERMAN, M.D., CALUMET CITY, ILL.

Before FULVICIN—tinea pedis of the soles caused by *Trichophyton rubrum.*



After FULVICIN—remarkable improvement in tinea pedis lesions after 3 months of oral treatment.

PHOTOS COURTESY OF HARRY L. WECHSLER, M.D., MCKEESPORT, PA.

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Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• UNEXPLAINED LEUKOCYTOSIS AND EOSINOPHILIA

Q. A colleague in Taiwan, Formosa, has requested advice on the diagnosis and treatment of the following case: A 10 year old boy was admitted to a hospital two and a half years ago because of a high fever of sudden onset. The boy's liver was enlarged three fingerbreadths below the costal margin, and bilirubin was increased to 3 plus, but there were no abnormal blood findings. A diagnosis of infectious hepatitis was made. During the two week period in the hospital, the patient was treated with methionine and AUREOMYCIN®, and he continued to have a low-grade fever. He was discharged, however, and instructed to rest at home and to continue taking Aureomycin.

Approximately three weeks after the patient was discharged, a repeat blood cell count was done because of persistent low-grade fever. The results of the test showed 12,000 white blood cells with 80 per cent eosinophils. Results of liver function tests appeared normal, but there still was no explanation for the leukocytosis and eosinophilia. ACTH and METICORTEN® were given on a trial basis, and the white blood cell and eosinophil counts gradually approached normal levels, remaining at 10,000 white blood cells with 10 per cent eosinophils for one year.

In June 1958, the patient was again admitted to the hospital with a white blood cell count of 21,000 and 63 per cent eosinophils. No therapy was initiated, and a natural remission began several weeks later.

In September 1959, the white blood cell count again increased to 25,000 with 10 per cent eosinophils. DECADRON® and BENADRYL® were administered, and the results were not too remarkable. The white blood cell count fell to 15,000 with 30 per cent eosinophils.

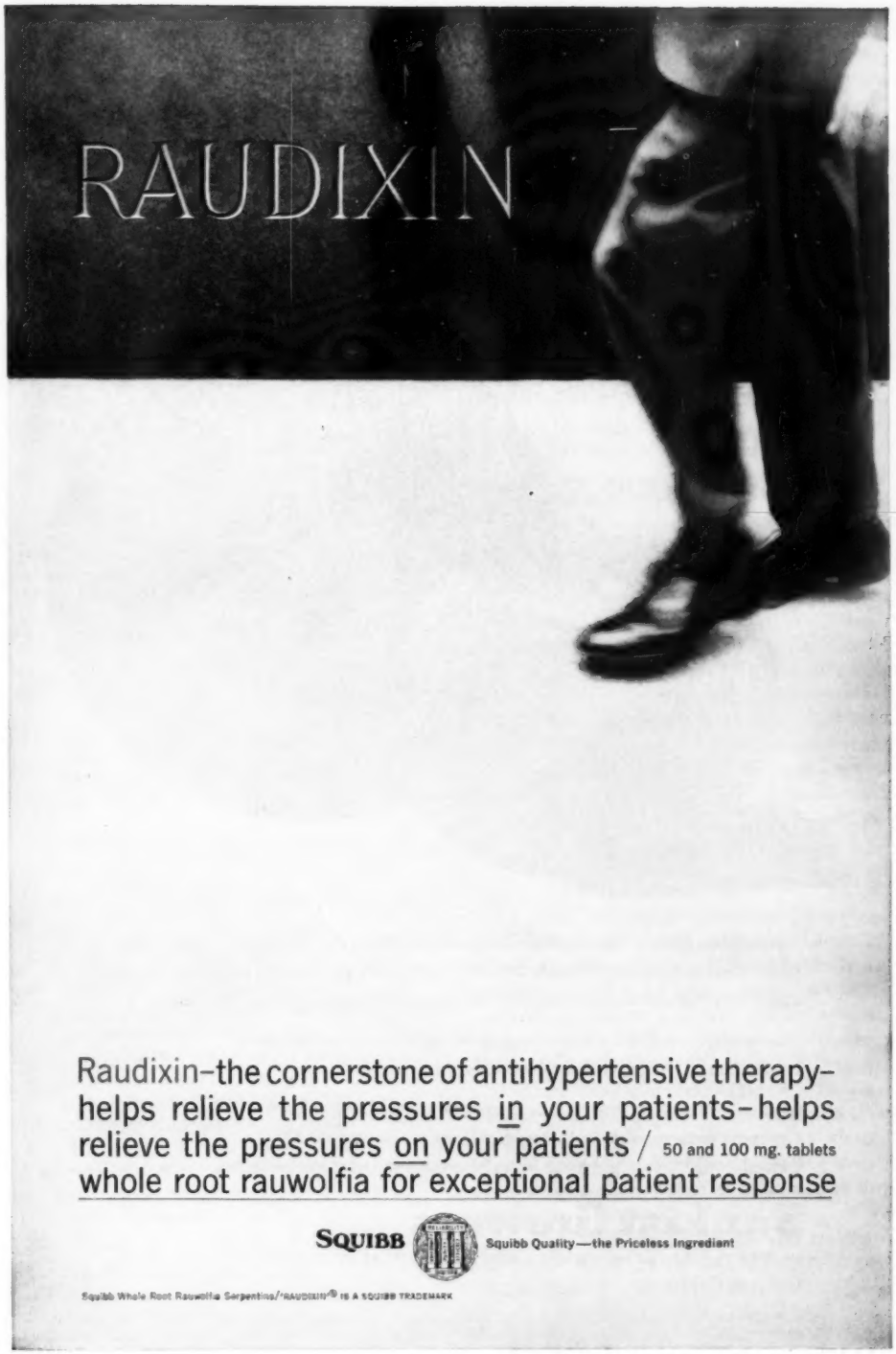
During these hospitalizations, repeated stool examinations for parasites gave negative results, as did x-rays of bones, examination of the cardiorenal system and spleen, and liver function tests. There was no evidence of general lymphatic glandular enlargement. Blood smears showed no abnormal young forms. Blood examination of the parents yielded negative results. There was no mention of a bone-marrow examination. Other significant findings included numerous eosinophils in the sputum and a spot of suspicious-looking infiltration in the left apex observed in x-rays of the thorax.

Despite these findings, the child was described as fairly well developed but slightly delicate. He has had some episodes of nasal congestion and bleeding and some infection of the conjunctivae, but no other complaints. The diagnoses entertained were: eosinophilic leukemia, tropical (?) (Taiwan is subtropical) eosinophilia, and allergic disorder.

M.D.—Rhode Island

A. On the basis of the data given it is not possible to assess accurately the meaning of the increase of bilirubin concentration to 3 plus, but this increase is regarded as significant and presumably is sufficient to cause visible jaundice. Tests of hepatic function are mentioned, but it is not disclosed what tests were used. This is an important consideration. After the first paragraph, there is no mention of the enlarged liver, so that it is not known whether the hepatomegaly persisted or abated. The persistent elevation of the leukocyte count and the large proportion of

(Continued on page A-21)



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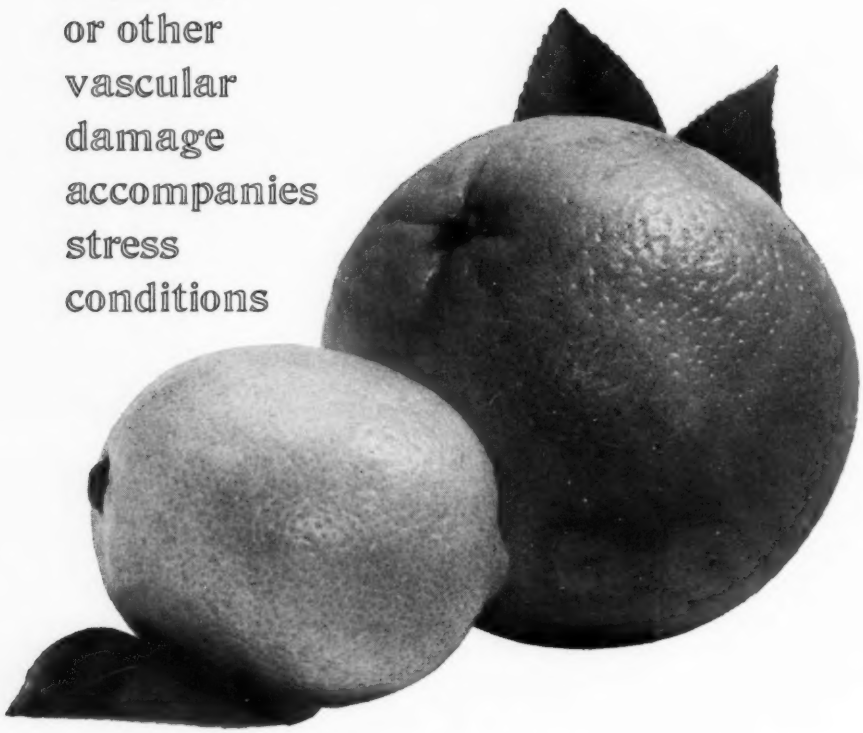
CITRUS BIOFLAVONOIDS

When capillary or other vascular damage accompanies stress conditions



Hesperidin, Hesperidin Methyl Chalcone, or *Lemon Bioflavonoid Complex* are prescribed as therapeutic adjuncts for control of vascular and capillary damage and abnormal cellular metabolism associated with many stress conditions.

These stress conditions may result from nutritional deficiencies, environment, drugs, chemicals, toxins, virus or infection.

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Disturbed capillary permeability and lowered capillary resistance, as well as the tendency toward edema and fluid retention, are well recognized in pregnancy (1, 2, 3, 4). The bioflavonoids have been shown effective in controlling the susceptibility to edema in pregnancy (5) and their routine prenatal use has been suggested (6).

Ecchymotic areas resulting from bruises and positive capillary fragility tests have frequently been observed in habitual aborters (7). Patients having a history of two or more spontaneous abortions have shown a marked improvement in fetal salvage after the addition of *Hesperidin* (a citrus bioflavonoid), ascorbic acid and other factors to the therapeutic regimen (8, 9, 12, 14, 15, 16). Other investigators have reported extensive use of the citrus bioflavonoids in the management of pregnancy with excellent results (18, 19, 20).

Observations include a reduction in severity or prevention of erythroblastosis fetalis in Rh-negative patients when *Hesperidin* (7) or other citrus bioflavonoids (23, 24) were administered.

The rationale of *Hesperidin* and other citrus bioflavonoids—in conjunction with vitamin C, nutritional factors or other therapeutic agents—as adjuncts in the management of pregnancy and its complications, spontaneous abortion and erythroblastosis fetalis, is based on the premise and observation that capillary involvement may be a contributing factor.

NOTE: For bibliography (B-688) write Sunkist Growers, Pharmaceutical Division, 720 East Sunkist Street, Ontario, California.

eosinophils certainly suggest some infectious process or parasites as a cause.

It is suggested that roentgenograms of the thorax be made at intervals so that migratory infiltrations, such as those which accompany Loeffler's syndrome, can be detected if they arise. A BROMSULPHALEIN® test should be done if it was not among the tests of hepatic function mentioned. Moreover, biopsy of the liver should be considered and examination of the bone marrow should be done. Skin testing is indicated to determine sensitivity to common environmental factors and pollens in the area.

In a case somewhat comparable to this one, a small boy had both leukocytosis and rather marked eosinophilia of more than 50 per cent which persisted for months and gradually receded. The significance of the hematologic observations never was ascertained, but it is assumed that a parasite was present which could not, at that time, be identified. The boy was seen more than 20 years ago, and since he eventually moved away, follow-up study was not possible.

• POSTINFARCTION TREATMENT

Q. How long should a patient receive anticoagulants following an acute myocardial infarction? Would it be for an indefinite period? What is the percentage of repeat infarctions in patients who had received this therapy compared with those who had received no anticoagulants?

Are drugs such as PERITRATE® of any prophylactic value following a coronary attack?

M.D.—Massachusetts

A. There is increasing evidence that anticoagulant therapy should be continued indefinitely following acute myocardial infarction. It is very difficult to give an exact percentage of repeat infarction in those patients who have been maintained on continued anticoagulant treatment as compared with those who have not been so treated. In general, however, subsequent infarction is about three times more common in the untreated patient, and the mortality rate is about eight times greater in those not receiving continuous anticoagulant treatment as compared with those who have been maintained on it.

To my knowledge Peritrate has no prophylactic value in the prevention of further myocardial infarction.

(Continued on page A-22)

• BORDERLINE HYPOTHYROIDISM

Q. As staff physicians in a university health center, my colleagues and I often see people who complain of tiredness and of becoming easily fatigued; constipation also is present in some cases. Generally, the results of a complete physical examination and the hematocrit reading are normal, but in many patients, the basal metabolic rate is low, ranging from –15 to –55. The determination of protein-bound iodine in some patients gives normal results; this finding was observed in one patient who had a basal metabolic rate of –55. Administration of thyroid medication apparently relieves the symptoms in some of these patients.

We also have seen patients of private physicians who have been started on thyroid therapy for similar symptoms and signs and who have remained asymptomatic. We have found that the basal metabolic rate generally remains normal while they continue taking thyroid; however, we have tapered the dosage of thyroid in some patients and after a suitable period have found that the basal metabolic rate is still within normal limits.

The textbooks do not seem to accept a state between euthyroidism and frank myxedema. I would like to know whether these patients are actually hypothyroid but not myxedematous or whether our calculation of the basal metabolic rate is in error. We have checked our calculations and have found no obvious source from which an error could arise.

M.D.—Utah

A. Attempts have been made to define this condition, and various terms, such as "metabolic insufficiency without hypothyroidism," have been coined to describe it. Many statements have been published attesting to the effectiveness of triiodothyronine in treating this condition. However, results of two excellent double-blind studies did not confirm this. The first investigation was carried out at the University of Minnesota by Dr. Sikkema (as yet unpublished), and the other was published in the *Journal of Clinical Endocrinology* (January 1960). These studies presented no evidence that thyroid, thyroxin or triiodothyronine benefits patients such as those whom you described. The incidence of relief was no greater with these medications than with placebos. It is highly probable, therefore, that so-called metabolic insufficiency is not a real entity. Without doubt, however, the best single test for borderline hypothyroidism is the determination of protein-bound iodine.

• BURSITIS

Q. Since 1953, a 37 year old man has had calcification of both shoulders and exostosis of the left elbow, confirmed by x-ray examination. Steroid therapy in adequate dosage did not relieve the weakness and pronounced fatigableness that occurred with slight exertion.

The patient has been receiving therapy with salicylates. What further treatment would be recommended for this condition?

M.D.—Pennsylvania

A. It is presumed that the calcification of both shoulders refers to calcific tendinitis or bursitis. Apparently, systemic steroid therapy and treatment with salicylates have not afforded sufficient relief. Appropriate measures of physical medicine should be employed; if these do not suffice, hydrocortisone injected locally or roentgentherapy should be tried. In some instances surgical removal of the calcific deposits may be indicated.

• PENICILLIN THERAPY

Q. Is there any good evidence, such as determination of the blood level, for using a certain type of penicillin in the treatment of otitis media, tonsillitis, etc.? I have used procaine penicillin G given daily or A-P BICILLIN® (a combination of procaine and benzathine penicillin G in aqueous suspension) given in one injection when the patient is first seen.

M.D.—Utah

A. Evidence of the efficacy of an antibacterial regimen usually is not correlated with the content of the agent in blood, but with the clinical course of the patient and the ultimate negativity of cultures. In situations in which penicillin is indicated, specifically when the infecting agent is a *Streptococcus*, procaine penicillin G given on alternate days for 10 days is satisfactory. Although it is perhaps less effective, benzathine penicillin G is administered to patients whose habits are such that they probably will not be available for the complete course of treatment with procaine penicillin G.

What's happening in Medicine

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

OVERHOSPITALIZED MENTAL PATIENTS

American Psychiatric Association:

• Studies show that psychiatric patients are sometimes harmed by being hospitalized too long. Treatment of grossly disturbed patients in the future may invoke brief hospitalization, during which family-oriented psychotherapy may begin, and be continued in an outpatient setting after the patient has been discharged.—Dr. Nathaniel S. Lehrman, Postgraduate Center for Psychotherapy, New York.

• Four separate investigations have shown that between 40 and 70 per cent of patients with psychoneuroses recover spontaneously within one to three years of the onset of symptoms. Recovery rates with psychotherapy are little greater. The processes of recovery, including the unlearning of old responses and the learning of new ones, are probably similar in treated and untreated patients.—Dr. Ian Stevenson, University of Virginia School of Medicine, Charlottesville.

INFLATING LUNGS STARTS HEART

Wisconsin State Medical Society:

• Experiments with dogs indicate that pumping oxygen into the lungs could raise blood pressure, increase the oxygen content of blood, and restart the heart in cardiac arrest. Pressure on the heart and large blood vessels from the inflated lungs apparently is responsible. However, the technic is not yet suitable for clinical application. Physicians are advised to continue their present resuscitation measures of opening the chest.—Dr. Jay Jacoby, Marquette University School of Medicine, Milwaukee.

LEUKEMIA-DIABETES LINK

California Medical Association:

• Postmortem material and clinical histories of 285 children with acute leukemia showed that 10 per cent had hypoglycemia, and that in 25 per cent of cases a member of the family, usually a grandparent, had diabetes. In persons used as controls, the incidence was only 4 per cent.—Dr. Daniel Stowens, University of Southern California School of Medicine, Los Angeles.

• In eight patients with acromegaly growth has been checked by treatment with alpha rays from a cyclotron. The dosage used does not destroy the pituitary.—Dr. Richard A. Carlos, Berkeley, Calif.

Placebo effect related to anxiety

Federation of American Societies for Experimental Biology:

- There is evidence that placebos are especially effective when the patient is worried and has great anxiety. The greater this anxiety is, the greater the effectiveness of the placebo. Brief pain produced experimentally in man is satisfactorily relieved by placebos in only about 3 per cent of cases, whereas pain arising from a pathologic condition is relieved in 34 per cent of cases. There is more anxiety in the pain of disease than in contrived pain.—Dr. Henry K. Beecher, Harvard Medical School, Boston.
- An experimentally induced deformity that resembles mongolism has been produced in animals for the first time. The deformity is produced by injecting fractions of human cancer cells into newborn hamsters. The relationship to human mongolism is unknown.—Dr. Helen W. Toolan, Sloan-Kettering Institute for Cancer Research, New York.

Predict survival time in leukemia

International Academy of Pathology and American Association of Pathologists and Bacteriologists:

- It is possible to predict the probable survival time of patients with chronic lymphocytic leukemia or leukosarcoma by laboratory measurements of the sensitivity of their white blood cells to x-rays. Statistics show a significantly lower survival time for patients whose white blood cells are resistant to irradiation.—Dr. Robert Schrek, Veterans Administration Hospital, Hines, Ill.

Drugs active against gastrointestinal cancer

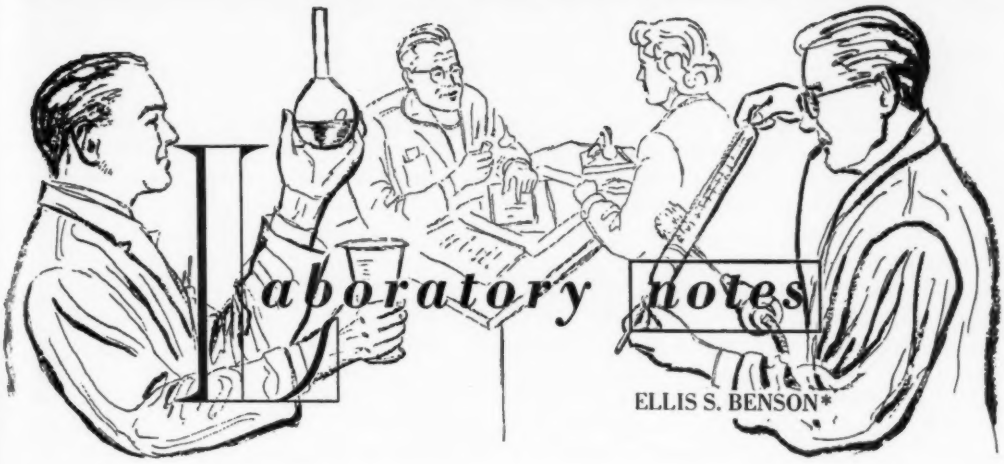
American Association for Cancer Research:

- Treatment with fluorinated pyrimidines (FU and FUDR) has produced anticancer activity in 48 per cent of a series of patients with cancer of the large bowel and substantial benefit in 11 per cent. The agents are the first known to restrain the growth of cancer of the gastrointestinal tract. The longest responses, with repeated courses of therapy, have been eight months in three patients. In the majority of patients, the response to treatment has been between three and five months.—Dr. C. W. Young, Memorial Center for Cancer and Allied Diseases, New York.

Chemoprophylaxis of tuberculosis

National Tuberculosis Association:

- Persons known to have been recently infected with tubercle bacilli should receive isoniazid as a protective measure. This would include young children who have a positive tuberculin reaction and children in a highly contagious environment who have a negative reaction, but who run a significant risk of contracting the disease. Among adults who should receive the drug are those who were previously treated for tuberculosis and left with extensive caseous residuals, those who had collapse therapy prior to the availability of drugs, tuberculin reactors who must receive corticosteroids for another disease for a long period of time, and individuals with a known history of tuberculosis who are faced with a prolonged debilitating illness.—Drs. H. Corwin Hinshaw, University of California School of Medicine, Berkeley-San Francisco, and William R. Barclay, University of Chicago School of Medicine, Chicago.
- A high incidence of cases of histoplasmosis has been found in tuberculosis sanatoriums in the United States, particularly in the central part of the country. A survey indicates that there may be between 3000 and 4000 cases.—Dr. Michael L. Furcolow, United States Public Health Service, Kansas City, Kan.



ELLIS S. BENSON*

Urinary Gonadotropins

In considering the subject of laboratory tests of gonadal function, one enters a field in which the methods are often so cumbersome, so time-consuming and so fraught with error that most clinical laboratories do not wish to attempt them. Only the determination of urinary 17-ketosteroids is widely used, and the value of this examination as a gonadal function test is sharply limited. It is useful only in men in whom low excretion rates may signify testicular deficiency but do not shed light on its nature. No method applicable to routine assay of urinary estrogens is currently available. Progesterone is assayed by estimation of urinary pregnanediol excretion, but this assay has not found wide clinical use and its diagnostic value is questionable. We are left then with the examination of urinary gonadotropin excretion, which is probably the most useful hormonal test of gonadal function. Since its estimation still depends on bio-assays, it is beset by all the inconveniences and inaccuracies accompanying the use of laboratory animals as test indicators.

The gonadotropins in human urine may be of either pituitary (HPG) or chorial origin (HCG). Agreement now exists that these gonadotropins are mixtures of the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH), and that the bio-assays clinically in use depend on the presence of both hormones. This fact complicates attempts to standardize clinical bio-assays through use of an international standard.

Undoubtedly, the most frequent application of the estimation of gonadotropins in human urine is in the diagnosis of pregnancy. HCG is excreted in high titer in the early weeks of pregnancy, reaching a peak between the fiftieth and seventieth days, after which it falls to a lower plateau level. Commonly used pregnancy tests based on the excretion of this hormone depend on its stimulating the formation of corpora lutea in the ovaries of immature female mice (Aschheim-Zondek test), ovulation in rabbits (Friedman test), and ovulation or spermatogenesis in frogs and toads (various tests).

The bio-assay of HCG is also useful in the diagnosis and management of tumors of placental origin, such as hydatiform moles and choriocarcinomas. Patients with these tumors may excrete very high levels of gonadotropin (HCG). This is also true of patients with certain carcinomas of the testis which apparently contain chorial tissue.

Human pituitary gonadotropin (HPG) is excreted in the urine of mature men and ma-

(Continued on page A-42)

*Director of Hospital Laboratories and Associate Professor of Clinical Laboratory Medicine and of Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

ture nonpregnant women. The amount excreted is of a completely different order of magnitude from that of HCG in early pregnancy. While the latter may be easily detected by bio-assay in unconcentrated urine, detection of HPG requires manifold concentration of urine. For example, in early normal pregnancy as much as 200,000 units of HCG (by rat ovarian hyperemia method) may be excreted daily,[1] while normal nonpregnant women of childbearing age excrete 5 to 30 units of HPG daily[2] (by the rat ovarian weight method). Although each of these depends on a different method of assay, the unitage is of roughly equivalent weight.

In what type of clinical circumstances is the assay of HPG useful? In general, it is clinically useful in the evaluation of precocious gonadal development in children and in gonadal deficiency in adults. Specific examples are as follows:

1. Precocious puberty—Most authors agree that HPG is not detectable in the urine of children before puberty and that it appears at puberty and rises gradually thereafter to adult levels.[2] When indications of sexual maturation appear in female children before the age of eight and in male children before the age of 10, precocious puberty is said to have taken place.[3] In isosexual precocious puberty, measurement of urinary gonadotropin excretion may help to distinguish between a hypothalamic-pituitary origin of the precocity and one resulting from a gonadal or adrenal tumor. In hypothalamic-pituitary precocity, the expected puberal rise of urinary gonadotropins may be found and the urine should then contain 2 or more mouse units of gonadotropin per 24 hours. This type of precocity may be the result of intracranial neoplasms, but it more commonly is of "constitutional" origin and therefore relatively benign.

2. Pituitary deficiency—Since urinary HPG is the one readily determinable pituitary hormone, its estimation offers a means of directly testing pituitary function. In panhypopituitarism, no detectable urinary HPG is found.[4] The success of attempted hypophysectomy in the treatment of hormone-dependent metastatic carcinoma of the breast has been judged by the assay of the urinary HPG.[5]

3. Hypogonadism—When gonadal deficiency antedates puberty, males may reach adulthood not only displaying failure of development of secondary sex characters (penis, scrotum, sexual hair, beard and deepened voice) but also perhaps showing certain abnormalities of body habitus. Among these are abnormal growth of long bones and female-type distribution of body fat, characters termed "eunuchoid." It is not possible to distinguish on the basis of the history or physical examination alone between eunuchoid individuals afflicted with primary testicular deficiency and those with primary isolated failure of pituitary secretion of gonadotropic hormones.[6] Estimation of urinary HPG will distinguish between these two groups, since those with primary testicular failure will have higher than normal levels of gonadotropin and those in whom hypogonadism is secondary to failure of pituitary secretion of gonadotropin will not have detectable HPG in their urine.

Klinefelter's syndrome is a hypogonadal syndrome in which testicular atrophy, gynecomastia, chromatin positivity and elevated urinary HPG are present. Chromosomal studies indicate that it is associated with an abnormal XXY sex chromosome complex.[7,8]

An example of hypogonadism in an individual who seems to be a female is the condition known as Turner's syndrome, in which sexual infantilism, short stature, other congenital abnormalities, chromatin negativity, and high urinary HPG levels are associated. This condition has been recently shown to be the result of an XO sex chromosome combination.[9] Because of the short stature and sexual infantilism, these individuals may be mistakenly considered to be pituitary dwarfs (panhypopituitarism). Determination of urinary HPG will point to the correct diagnosis, as will examination of the chromatin pattern on buccal smear.[8]

Postmenopausal women commonly excrete increased amounts of HPG, and Albert's[2] studies indicate that the excretion varies markedly from day to day.

Chemical methods of estimating HPG have

(Continued on page A-44)

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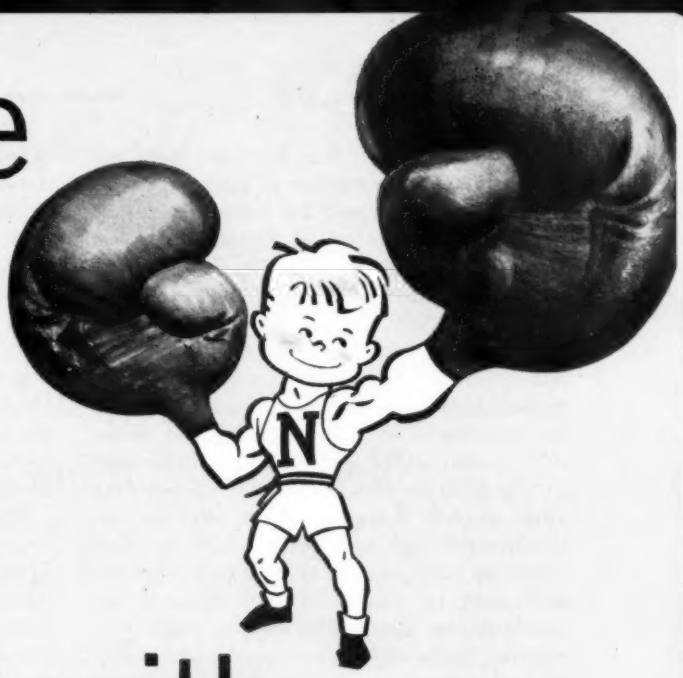

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Phenylpropanolamine HCl	20 mg.	20 mg.	40 mg.
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Chlorpheniramine maleate	2.5 mg.	2.5 mg.	5.0 mg.

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been attempted but, thus far, have been unsuccessful. A large number of bio-assay methods are in use. These differ from one another chiefly in the method of extraction of the hormone from the urine and in the choice of biologic measure of activity. A method of extraction recently developed by Albert[2] and suited especially to large-scale testing employs adsorption of the hormone on kaolin and filtration under pressure. Most commonly, some modification of an alcohol-precipitation method[10] is used. HPG is precipitated from urine by the addition of 4 volumes of 95 per cent ethyl alcohol. Estrogen, which may be coprecipitated and may give a false positive result in some assays, is removed from the precipitate by washing it with ether. If the precipitate is then redissolved in water and injected, in the high concentrations which may be necessary to detect HPG it will be toxic to the test animals and may cause their death before the test is complete. A number of methods have been used to reduce this toxicity. One of these is to redissolve the precipitate in 50 per cent ethyl alcohol (in which HPG is soluble) and then to reprecipitate the gonadotropin by raising the alcohol concentration to 80 per cent.[11]

A favorite biologic measure of activity of HPG is the ability to stimulate an increase in uterine weight in the immature female mouse. This is a sensitive assay but lacks specificity, since it depends on stimulating the mouse ovary to secrete estrogens. Thus, estrogenic substances must be completely removed from the urine concentrate before assay. A more specific assay employs increase in the weight of ovaries in immature rats.[2]

More details concerning extraction technics and the fine points of bio-assays may be found in the papers cited[10,11] and in the reviews by Albert[2] and Loraine.[4] In our hands, the bio-assay is only semiquantitative, and low, normal and high excretion levels may be distinguished from each other.

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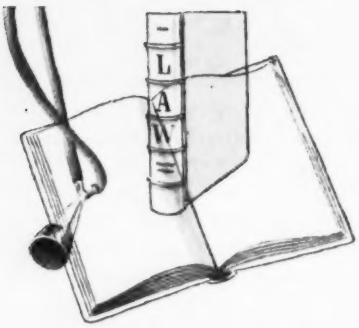

Forensic Medicine

Chest Injuries in Automobile Accidents

LAURENCE H. RUBENSTEIN*

Chicago Medical School, Chicago

LAURENCE H. RUBENSTEIN

In this era of high-speed motor vehicles, the human passenger frequently may become the injured victim of an automobile crash. It is beyond the scope of this presentation to discuss the cause of accidents, many of which are probably avoidable. The safety engineers, traffic experts and psychologists often have pointed out the dangers of high-speed travel, road conditions, motorist fatigue, psychologic immaturity of drivers, and other factors which play such important roles in this growing national problem. The rising toll of deaths from automobile accidents is appalling. The immediate cause of death in many cases is directly attributable to a chest injury. The vital structures lying within the bony rib cage must receive prompt, alert and adequate attention.

Mechanism of Injury to the Chest

When a driver or passenger in a high-speed vehicle receives a chest injury, it is in one of the following ways. A speeding car crashes; when it comes to an abrupt stop, the contents and passengers in the car are still moving, carried forward by momentum. The driver is thrown against the steering wheel or dashboard, and the passengers hit the dashboard or other parts of the car (figure 1). The doors of the car fly open and passengers are thrown from the car, or an overturned car may pin the passenger beneath it. The severity of the injury is commonly proportional to the speed at the time of impact. To be sure, it is common for the injured persons to have other severe injuries associated with those of the chest. Injuries to the head, the intra-abdominal region and the bones add to the complexity of managing such cases.

Prophylaxis of Chest Injuries

If the driver or passenger could retain his position in the automobile when it comes to the abrupt stop in a crash, he might avoid the sequela of being thrown against a firm surface and might thus escape serious injuries. When an impending impact faces the persons in an automobile, they may brace themselves, but unless they are fixed in their seats their momentum will carry them forward to almost certain injury. The logic of safety belts therefore is to retain the occupant in the seat so

(Continued on page A-60)

*Department of Thoracic Surgery, Chicago Medical School and Michael Reese and Mount Sinai Hospitals; Consultant Thoracic Surgeon, Hospital of St. Anthony de Padua and Louis A. Weiss Memorial Hospital, Chicago, and Kankakee State Hospital, Kankakee, Illinois.

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IN HYPEREMOTIVE ADULTS does not impair mental acuity	"... especially well-suited for ambulatory neurotics who must work, drive a car, or operate machinery." Ayd, F. J., Jr.: New York J. Med. **57**:1742 (May 15) 1957.	Garber, R. C., Jr.: J. Florida M. A. **45**:549 (Nov.) 1958. Menger, H. C.: New York J. Med. **58**:1684 (May 15) 1958. Farah, L.: Internat. Rec. Med. **169**:379 (June) 1956.

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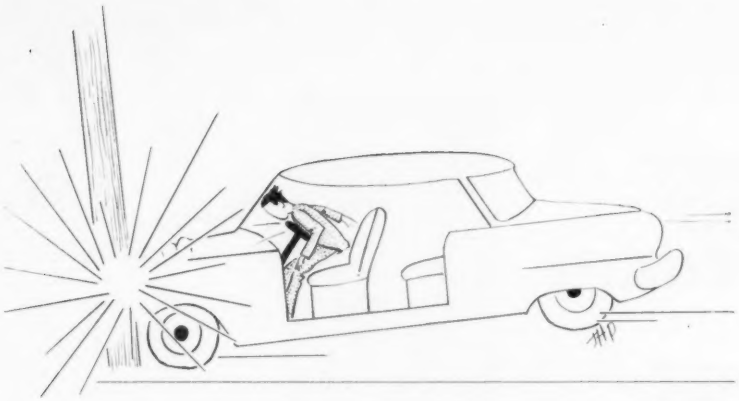


FIGURE 1. Drawing illustrating the manner in which chest injuries commonly result when an automobile stops abruptly.

that he can avoid being hurled forward. Seat belts have proved their value in many instances. If seat belts are not used, a person seeing an impending crash may grab an automobile cushion and place it between himself and the steering wheel or the dashboard. He may cross his arms in front of his chest and try to absorb the greater part of the blow in a less vital portion of the body. Persons sitting in the rear seat usually will receive less injury than will those in the front seat. The passenger can brace himself against the softer impact-absorbing back of the front seat. Indeed, a passenger in the rear seat may slip to the floor of the car and avoid injury by fixing himself to the back of the front seat.

Types of Injuries to the Chest

Nonapparent injuries—Even though the chest absorbs the maximal force of the impact there may be no grossly demonstrable lesion. Before one can dismiss the chest injury, he must make certain that hidden damage is not overlooked.

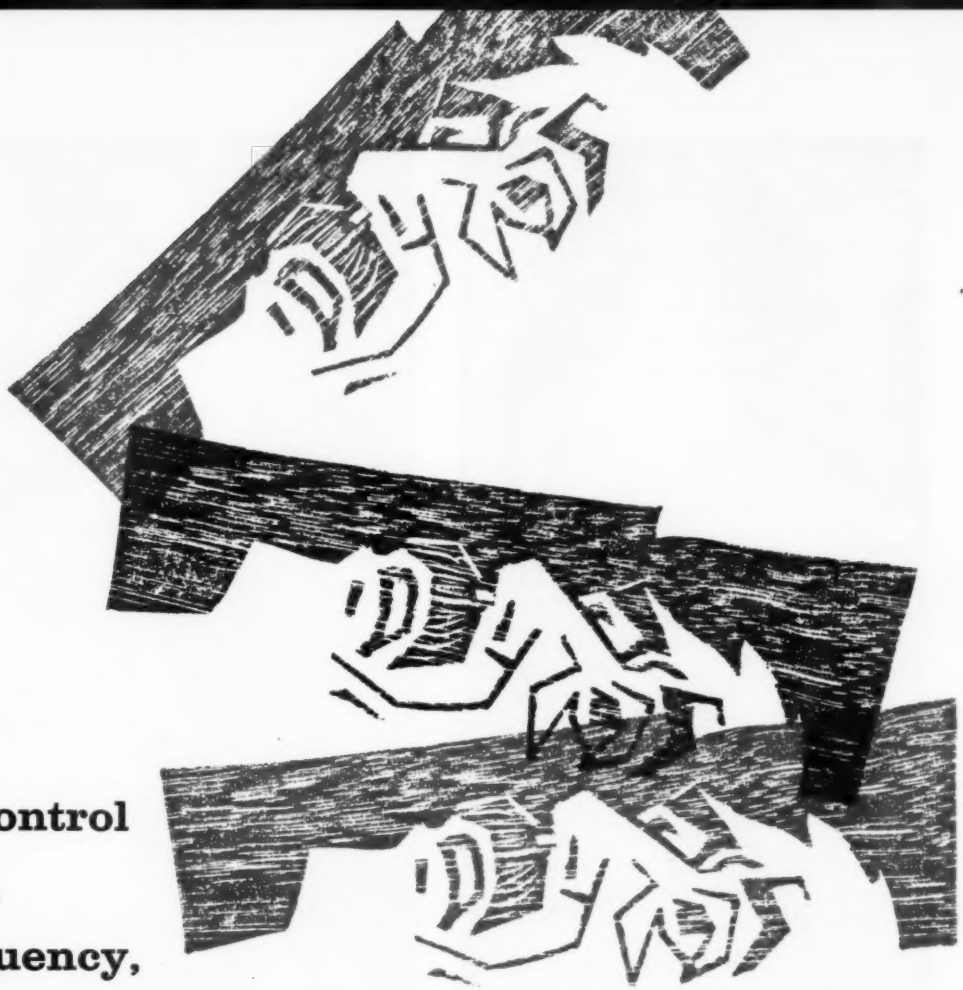
By inspection, palpation and auscultation, soft-tissue injury may be noted. Point tenderness and crepitation may reveal a bony injury. Absent breath sounds or cardiac irregularities may suggest visceral damage. Some persons may seem to have no injury, but they should not be dismissed until an x-ray of the chest and an electrocardiogram are made.

Contusion of the lung—A contusion of the lung may occur without any external signs. A portion of the lung may become hemorrhagic and edematous, and an x-ray opacity will be noted, as demonstrated by the following cases.

Case 1—A 12 year old white boy sustained a chest injury with no referable complaints. The major area of complaint was the head. The patient had transient unconsciousness and swelling and ecchymosis of the left eye. A day after the injury a chest x-ray revealed a 2.5 cm. rounded opacity. The patient remained remarkably free of chest symptoms. Over a 12 week period, this area of pulmonary contusion underwent progressive resolution, changing from dense opacity to an excavated lesion and finally clearing (figure 2a, b and c). Contusion of the lung may be associated with hemoptysis and dyspnea and complicated by sepsis in some cases.

Case 2—Symptoms of chronic cough and bouts of hemoptysis developed in an 18 year old white boy within a period of two to three months after he was injured in an automobile accident. On two occasions the hemoptysis was in excess of 300 ml. of bright red blood. With each upper respiratory infection a productive cough and fever developed. X-rays of the chest revealed residual pulmonary infiltration, with evidence of cavitation in the superior segment of the right lower lobe (figure 3a and b). Because of the persistence of posttraumatic residual infection with excavation which bled frighteningly, surgery was per-

(Continued on page A-62)



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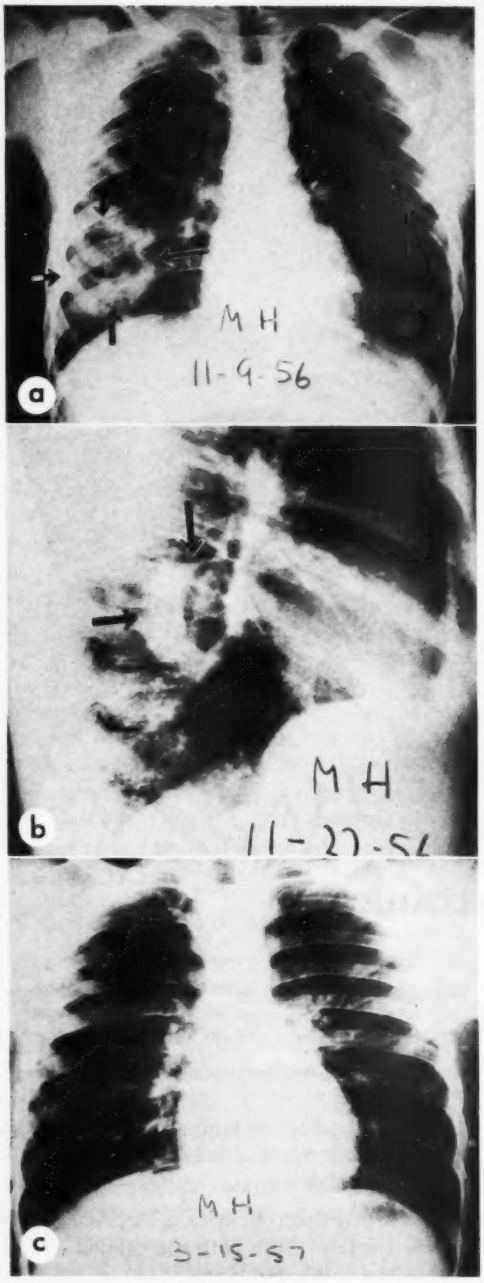

FIGURE 2. Case 1. a. Posteroanterior view of the chest showing an area of excavation in the lower lobe of the right lung. b. Lateral view of the right lower lobe showing post-traumatic cavity. c. X-ray made four months after the injury showing complete clearing of lesion.

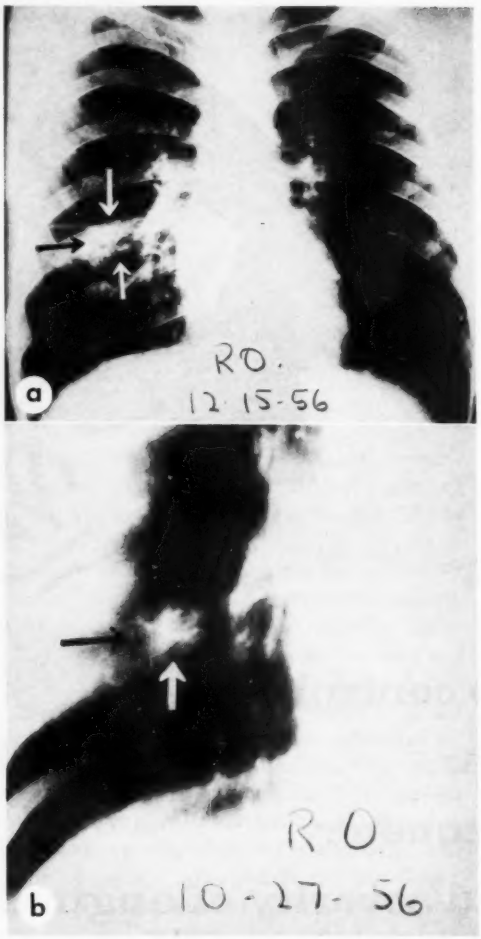

FIGURE 3. Case 2. a. X-ray showing residual area of infection in the lower lobe of the right lung eight months after the patient was injured in an automobile accident. b. Laminagram of the infiltrated area of the right lower lobe, which was the source of hemoptysis.

formed. An excellent clinical result was obtained from a segmental resection of the superior segment of the right lower lobe.

Contusion of the heart and great vessels—It is easy to understand how the heart, even though it is protected by a bony cage, may not escape injury. This is commonly overlooked. While a patient may have no symptoms, he will show objective findings such as electrocardiographic changes revealing injury

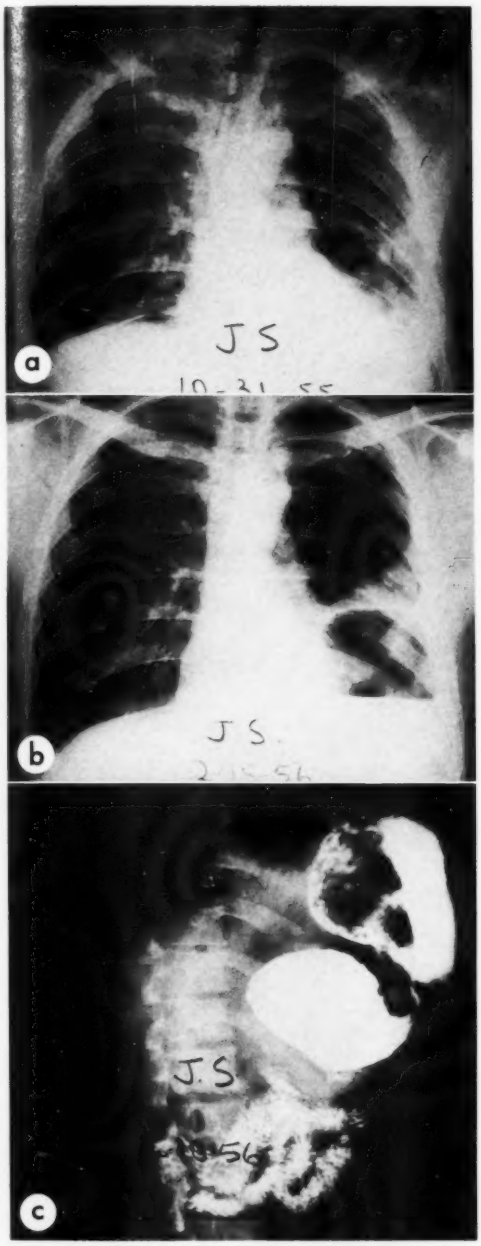

FIGURE 4. Case 4. a. Posteroanterior view of the chest showing initial trauma to the left side of the chest, with multiple rib fractures and hemopneumothorax. b. X-ray made 14 weeks after the original injury showing stomach incarcerated in the left side of the chest. c. Barium in the stomach showing the proximal half of the stomach incarcerated in the left side of the chest.

patterns. The injury may vary from mild contusion to rupture of the heart or great vessels. The following case is an example of myocardial damage.

Case 3—A 30 year old white man who was driving a pie truck while in a standing position was thrown free of the truck when it collided with an automobile. The truck, however, fell over on its side and pinned the driver across his chest. He arrived at the hospital in good condition; gross findings showed only a small soft-tissue injury to the right anterior portion of the chest at the fourth costosternal junction. Chest x-rays were normal; there were no fractures. The patient had no complaints except for a "bruised feeling" in the chest. Electrocardiograms showed a progressive pattern of myocardial damage. He was kept at bed rest for three weeks until the pattern of injury began to heal. He has continued to be free from symptoms.

Rupture of the diaphragm—Any of the intrathoracic viscera may be affected by direct or indirect trauma. The tremendous force of a blow to the chest and abdomen may release itself via a tear in the diaphragm. The patient may have relatively few, if any, symptoms referable to the diaphragm. Associated injuries of bones or lung and other viscera may obscure the clinical picture at the time of accident. At a later date the patient may have symptoms of upper gastrointestinal distress. X-ray studies will reveal abdominal contents pushing through the diaphragm. The viscera may become incarcerated and obstructed, as illustrated by the following case.

Case 4—A 32 year old white man encountered trauma to the chest, with fractured ribs and scapula and hemopneumothorax (figure 4a). He was treated with injections in the intercostal nerve to relieve the pain from the fractured ribs, thoracentesis to evacuate the blood in the left side of the chest, aerosol bronchodilators, and antibiotics. He made a good recovery. Twelve weeks after the initial injury he had dysphagia, anorexia and vomiting. X-rays showed an incarcerated stomach through a diaphragmatic defect (figure 4b and c). At thoracotomy the incarcerated and

(Continued on page A-66)

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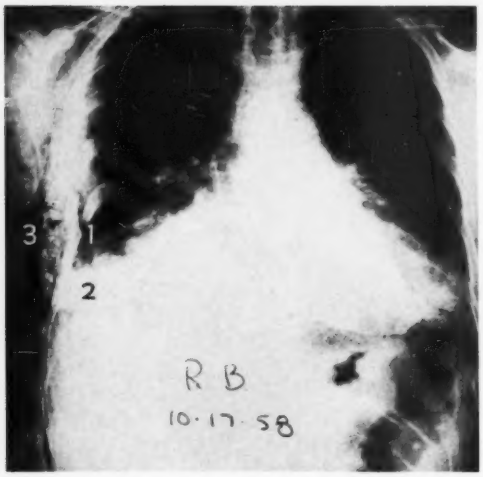

FIGURE 5. X-ray showing multiple rib fractures, hemothorax and subcutaneous emphysema resulting from a crush injury to the left side of the chest. Paradoxical motion was present in the lower right side of the chest.

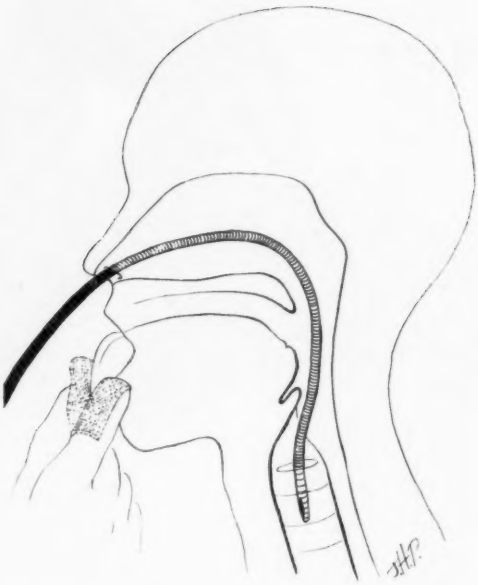

FIGURE 6. Drawing showing transnasal endotracheal suction, a simple, sometimes lifesaving procedure. Note that the tongue is pulled forward and the catheter is advanced during inspiration.

twisted cardia and fundus of the stomach were found to project through a tear in the central portion of the left leaf of the diaphragm. The viscera were reduced into the abdomen, and the left leaf of the diaphragm was repaired. The patient is now clinically well.

Apparent injuries—A patient often is brought to the emergency room with marked respiratory distress, gasping, in extreme pain, and coughing up blood. It is obvious that there is intrathoracic injury. This may include fractured ribs, a fractured sternum (from being crushed against the steering wheel), flail chest with bilateral rib fractures, pneumothorax, hemothorax, or hemopneumothorax. It is imperative that an accurate diagnosis be made as soon as possible. It is not enough to give oxygen and treat the shock; one must try *as quickly as possible to restore normal physiologic function of the thorax.*

By inspection and palpation one may note subcutaneous emphysema, paradoxical motion of the chest, or obvious inadequate aeration of a lung. Point tenderness may localize fractures of the ribs and sternum (figure 5).

Auscultation may reveal absent breath sounds on one side of the chest. Hyperresonance may suggest pneumothorax. An x-ray of the chest should be made as soon as it is feasible. If the patient is desperately ill, a portable x-ray may suffice to establish the presence of pneumothorax, hemothorax, tension pneumothorax with mediastinal shift, fracture and dislocation of the ribs and sternum, mediastinal emphysema, or defects of the diaphragm. When the patient can be moved to the x-ray department, a more suitable chest plate might give more accurate information regarding the extent of injury. When pneumothorax is suspected, it is always advisable to make a chest film during expiration in addition to one made during inspiration; the former may show the pleural air when the latter does not.

The desperately injured person requires careful, prompt attention, and an early, proper approach will make the difference between survival and death. It is axiomatic that the shock be treated at once with intravenously

(Continued on page A-68)

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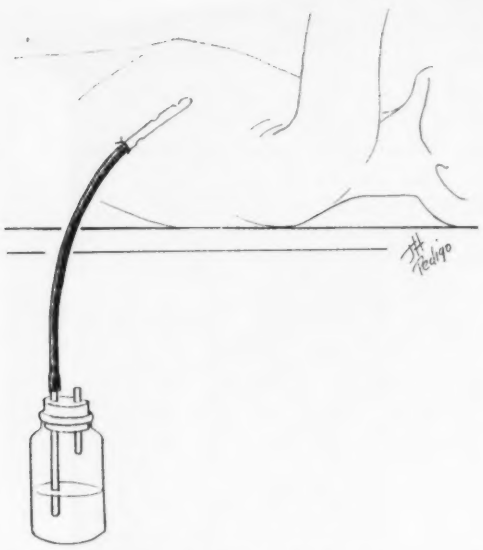


FIGURE 7. Drawing showing a simple underwater-seal catheter drainage.

administered fluids, blood substitutes, plasma or blood.

Basic Principles of Treating Chest Injuries

When it is apparent that the patient cannot breathe because of severe chest injury, the following basic principles should be considered.

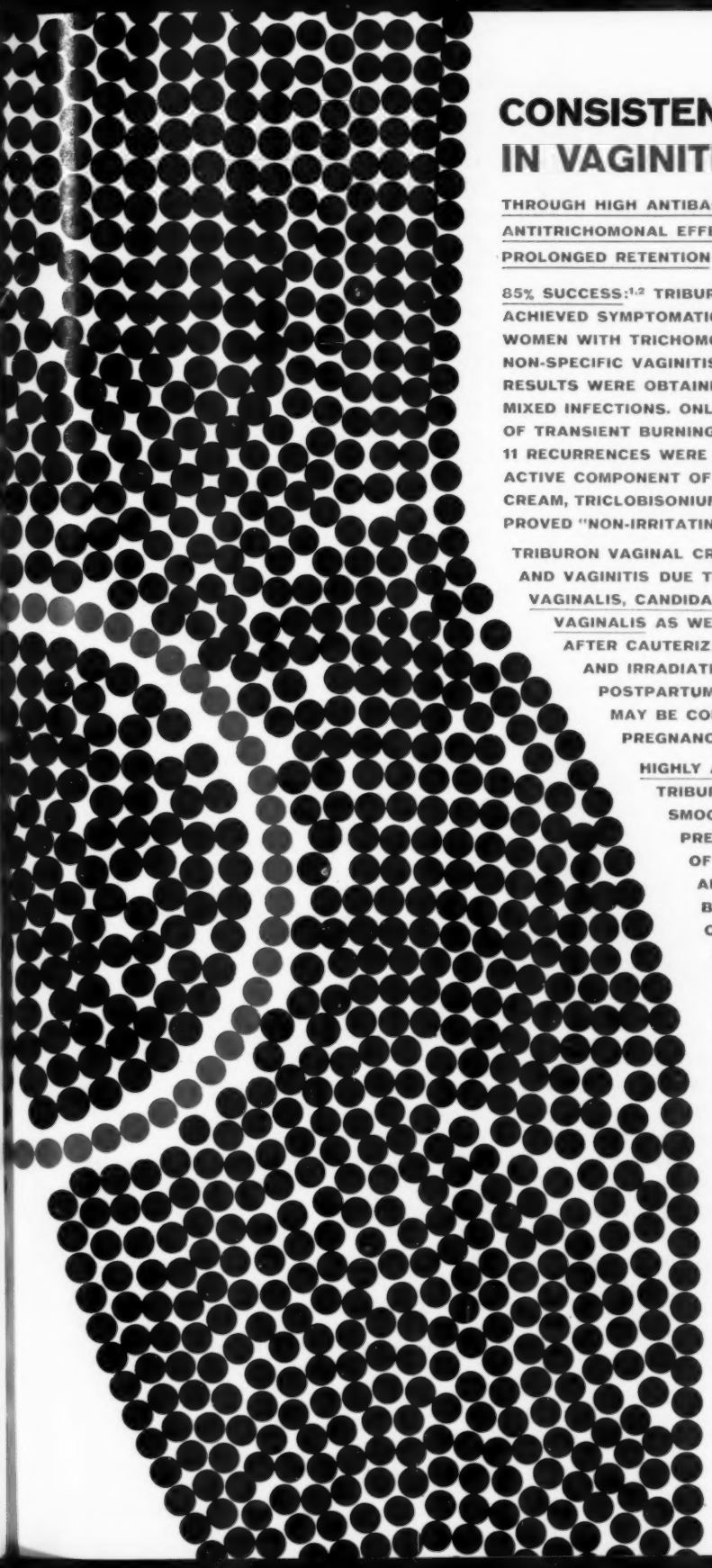
1. *Establish and maintain a clean airway as quickly as possible.* The technic for this procedure will vary with the cause of the airway obstruction. If the jaw and tongue fall back to occlude the glottis, elevation of the angle of the mandible and insertion of an anesthetist's airway may suffice. When the trachea is blocked with blood and thick secretions, the trachea may be aspirated by passing a catheter with suction beyond the vocal cords (figure 6). If an anesthesia endotracheal tube is available, it may be passed temporarily to clean and maintain the airway. Oxygen can then be supplied via this tube. When it is obvious that repeated aspirations of the trachea will be necessary or if the chest is flail and no adequate function of the chest wall is exhibited, a tracheostomy is a simple, direct, good procedure for establishing an airway, keeping the tracheobronchial tree clean, and decreasing the "dead space" between the pharynx and the lung. If it can be a deliberate procedure, it is more favorable than one which must be done within minutes while a patient is gasping.

Bronchoscopy and aspiration of obstructed bronchi may be carried out when it appears that such a procedure will give the desired relief of the obstruction. If repeated bronchoscopic aspiration is necessary, it is best to establish a tracheostomy.

2. *Effect early and complete expansion of the lung.* If pneumothorax is present it may be minimal or complete. It may be associated with hemorrhage (hemopneumothorax), and it may be rapidly progressive, with a persistent air leak from the lung. The most desirable treatment is to effect catheter thoracostomy drainage with underwater seal for evacuation of air and fluid (figure 7). As soon as the air space in the pleural cavity is emptied, there will be increased pulmonary function and a decreased possibility of intrapleural complication. In the majority of cases, response to this treatment will be good. The catheter drainage may be performed in an intercostal space with the patient under local anesthesia. A large-sized catheter (No. 20 to No. 30 French) has less tendency to become obstructed with clot and fibrin.

3. *Restore function as promptly as possible to the injured bony cage.* In a flail chest which moves paradoxically during respiration, pulmonary ventilation is markedly impaired. A paradoxical chest wall is one which moves inward during inspiration (because the bony rib fragments are broken at two places), when the chest normally should be expanding. Conversely, when the patient exhales the chest wall should collapse, but the flail portion of the chest will move outward. In the emergency room a flaccid chest wall can be immobilized by placing sandbags against that portion of the chest, or, if it is a truly staved-in chest, towel clips may temporarily be placed to lift the loose chest wall. Traction may be applied by many technics to allow the chest wall to be fixed. In a severely crushed chest it is a life-

(Continued on page A-70)



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REFERENCES: 1. H. MULLA AND J. J. McDONOUGH, ANN. NEW YORK ACAD. SC., 82:(ART. 1), 162, 1959. 2. L. E. SAVEL, D. B. GERSHENFELD, J. FINKEL AND P. DRUCKER, IBID., P. 186. 3. R. C. V. ROBINSON AND L. E. HARMON, ANTIBIOTICS ANNUAL 1958-1959, NEW YORK, MEDICAL ENCYCLOPEDIA, INC., 1959, P. 113.

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saving procedure first to establish a tracheostomy and secondly to provide intermittent positive pressure via a mechanical respirator so that there is adequate ventilation. A very suitable respirator has been that of the Mörch[1] type, which delivers positive pressure to the tracheostomy tube and keeps the chest wall immobile. The patient is relatively free of pain and can be kept well ventilated.

Lesser injuries to the bony cage can be treated by applying sandbags to the chest wall or preferably by injecting a local anesthetic into the intercostal nerve.

4. *Avoid any process that would interfere with good pulmonary ventilation.* This means to *avoid narcotics* which depress respiration and the cough reflex. If necessary, give narcotics sparingly only when it is certain that the airway is clean and unobstructed. *Avoid heavy taping of the chest wall for immobilization*; this keeps the lung from adequately aerating. These statements are really a corollary to the first major principle, namely, to keep the airway clean and unobstructed.

When the patient can cooperate, he is instructed to cough and expectorate frequently. In order to avoid atelectasis and subsequent pneumonitis, prophylactic antibiotic and aerosol bronchodilators are given. The nebulized solution (e.g., 2 ml. saline plus 1:200 ISUPREL®) is administered until the danger of atelectasis is eliminated. Careful attention to tracheobronchial cleansing has eliminated many of the serious pulmonary complications following injury.

Complications

With knowledge of the expressed basic principles in chest injuries, one will avoid most serious complications. There are, however, serious sequelae which might be mentioned.

Pneumonitis and abscess formation—Localized injury or atelectasis in a segment or lobe of the lung (figure 3a and b) may cause pneumonitis and formation of an abscess. Careful attention to keeping the tracheobronchial tree cleansed by cough, expectoration, bronchoscopic aspiration and aerosol inhalation plus antibiotics should control the problem in most instances.

Hemothorax and fibrothorax—Hemothorax must be treated by complete evacuation of the blood and fluid from the pleural space. Thoracentesis may be repeated as necessary until the fluid is gone. When the fluid is excessive and occupies more than one-third of the hemithorax, an underwater catheter drain will accomplish the evacuation more quickly and thoroughly. The healing process produces fibrothorax. A heavy layer of thick, binding scar "captures" the lung and causes shrinkage of the hemithorax, with impairment of pulmonary function. Infection in the space with formation of empyema may cause the same serious problem plus sepsis. The treatment now is surgical. The heavy cortical scar must be removed and "peeled away" to restore maximal lung function.

Persistent air leak—In spite of catheter drainage of the pleural space, air may continue to leak and plague the patient. If after 10 days to two weeks significant bubbling continues in the underwater-seal bottle, the treatment may be a thoracotomy with repair of the area in the lung or bronchus which continues to leak air.

Other serious complications have been mentioned. Trauma to the heart or great vessels may cause progressive aneurysm with eventual rupture. When this process is recognized, surgical repair is imperative. Rupture of the diaphragm should be repaired by surgery when the condition is recognized.

Summary

Automobile accidents, with associated serious chest injuries, are increasing in frequency. Injury to vital viscera of the chest is a common cause of death. The mechanism of injury, the prophylaxis, and the basic principles which must be understood and applied to save lives have been discussed. Prompt, effective therapy will decrease complications and mortality in most instances.

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Radiology FOR PRACTICING PHYSICIANS

PAUL C. HODGES*

Myelography

KLAUS RANNIGER

University of Chicago, Chicago

Dr. Ranniger was born July 4, 1926, in Hamburg, Germany. He received his M.D. degree from the University of Kiel in 1951. This was followed by a three year period as resident in internal medicine at the University of Kiel and nine months as resident in the department of pathology at the University of Cologne.

On July 1, 1955, Dr. Ranniger came to the University of Chicago to begin residency training in radiology. In May 1958, he passed the examination of the American Board of Radiology, and is now an instructor in the department of radiology at the University of Chicago.—Paul C. Hodges, M.D.

ALTHOUGH, admittedly, myelography is an x-ray examination which is best done by teams of well-qualified radiologists and neurosurgeons and never by practicing physicians as a routine part of a neurologic examination, it is well for all physicians to have an understanding of its scope and limitations. Myelography is the fluoroscopy and filming of the radiologically invisible spinal cord and subarachnoid space with the aid of negative contrast media,[1] that is, gases (usually air), or, much more commonly, with the aid of positive contrast media,[2-8] of which the oily PANTOPAQUE® is by far the most commonly employed. Water-soluble opaque media have found little favor in this country.

KLAUS RANNIGER

Technic of Examination

Ordinarily, a 20 gauge spinal needle is introduced into the spinal canal at the level of the L3-L4 interspace with the patient in the sitting position; 10 to 12 cc. of Pantopaque is injected, following which the needle is removed. Under certain circumstances the injection is made at other levels. The patient is then placed on a tilting fluoroscope and is tilted into various positions; this maneuvers

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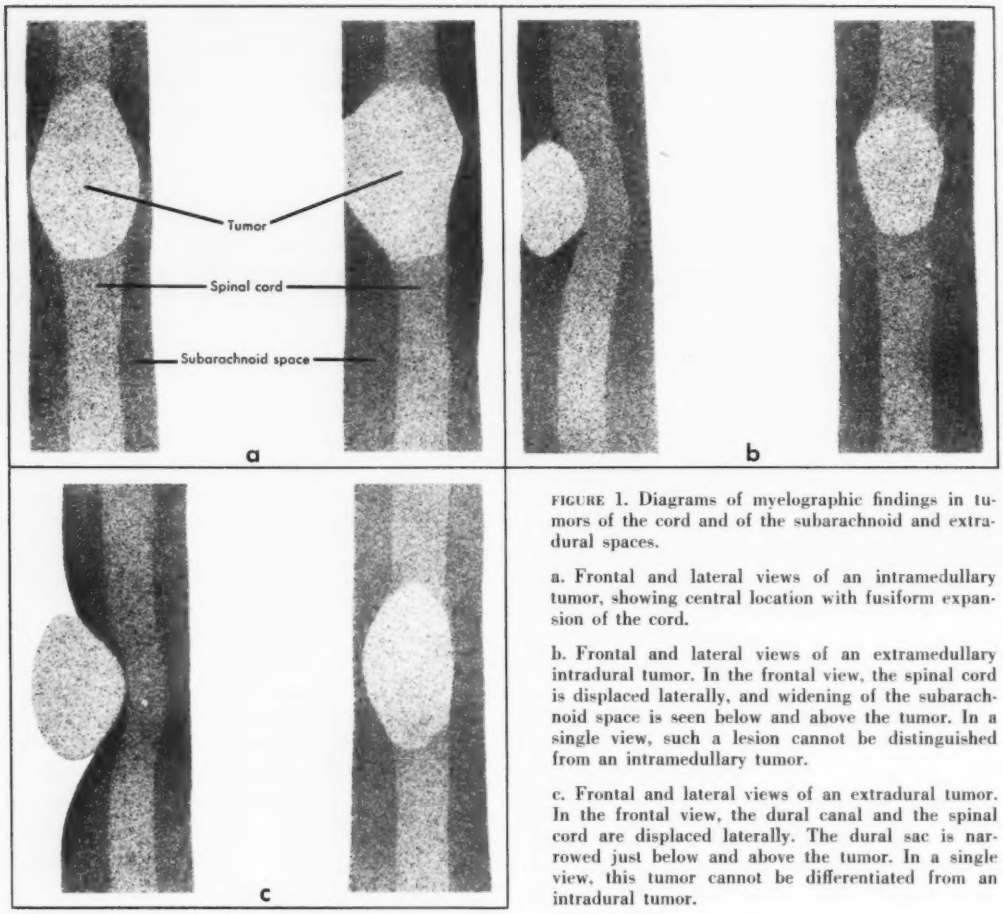

FIGURE 1. Diagrams of myelographic findings in tumors of the cord and of the subarachnoid and extradural spaces.

a. Frontal and lateral views of an intramedullary tumor, showing central location with fusiform expansion of the cord.

b. Frontal and lateral views of an extramedullary intradural tumor. In the frontal view, the spinal cord is displaced laterally, and widening of the subarachnoid space is seen below and above the tumor. In a single view, such a lesion cannot be distinguished from an intramedullary tumor.

c. Frontal and lateral views of an extradural tumor. In the frontal view, the dural canal and the spinal cord are displaced laterally. The dural sac is narrowed just below and above the tumor. In a single view, this tumor cannot be differentiated from an intradural tumor.

the Pantopaque until it has outlined the entire subarachnoid space. In the normal patient the Pantopaque will flow freely and the entire canal will fill, including the nerve-root pouches. When at fluoroscopy one detects a lesion interfering with the free flow of the Pantopaque, an attempt is made to pass the opaque material beyond the lesion in order to outline its entire periphery. Of course, when the obstruction is complete, this cannot be done and a second injection may have to be made at a point well above the supposed upper limit of the lesion. Large masses are seen easily, but small ones are apt to be overlooked at fluoroscopy. Therefore, so-called spot films are made throughout the course of the fluoroscopic examination, not only of regions under suspicion but also throughout the course of the spinal canal. The filming must be done in the frontal, lateral and oblique positions. After completion of the examination the contrast medium is removed under fluoroscopic control. Myelography is contraindicated immediately following most injuries of the spine; of course, if the clinical condition requires laminectomy for decompression, direct inspection becomes possible at the time of operation.

In addition to performing subarachnoid myelography as described here, some workers inject water-soluble contrast media into the epidural space (epidural myelography) or inject gas into the subdural space (subdural

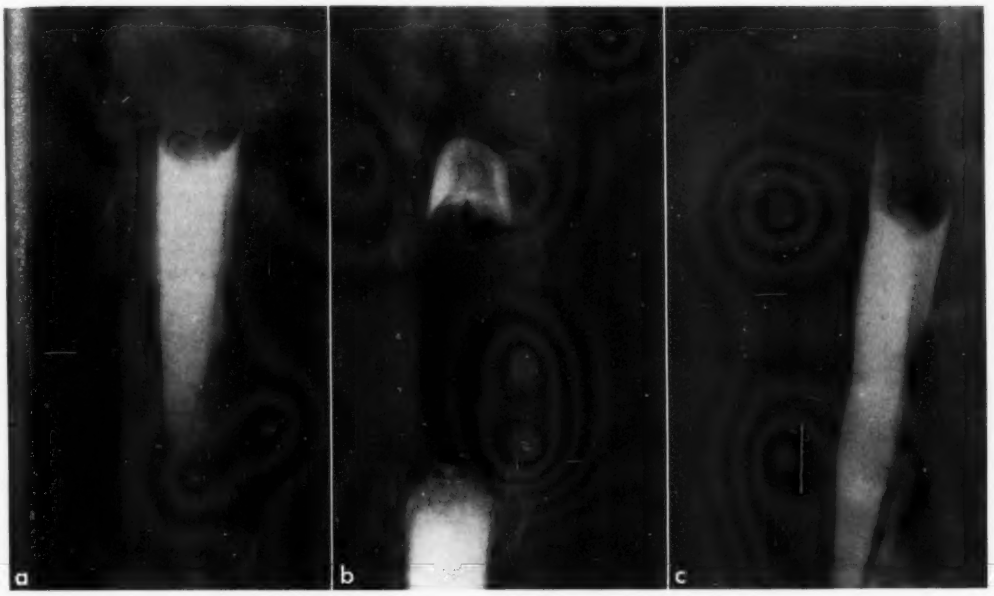

FIGURE 2. a. Frontal view of an intramedullary glioma, showing lower border of tumor. This x-ray was made with the patient's head down.

b. Frontal view made with the patient's head up, showing upper border of tumor.

c. Lateral view made with the patient's head down, showing central location of tumor with fusiform enlargement of the cord.

myelography). Both procedures are of questionable value.

Evaluation

Abnormal masses may be within the cord itself, outside the cord but within the dura mater, or outside the dura mater. Usually, such masses are neoplasms, but similar changes sometimes are caused by abscesses, congenital malformations or even trauma. It is usually possible to determine by myelography whether a lesion is within the cord or subarachnoid space or outside the dura mater (figure 1).

Intramedullary Masses Expanding the Spinal Cord

In all projections such masses lie approximately in the center of the canal and produce a fusiform defect (figure 2). If a tumor is of moderate size it will not touch the wall of the spinal canal at any point. If the examination is confined to a single plane, an extradural mass may appear to lie within the cord. Intramedullary tumors sometimes are accompanied by increased vascularity, and large tortuous vessels can be seen at the surface of the cord.

The most common intramedullary tumor is the glioma. Vascular malformation, hemorrhages and abscesses expand the cord in much the same manner as tumors do. In syringomyelia the segment of enlarged cord is usually much larger than it is in tumors (figure 3).

Extramedullary-intradural Tumors

These tumors are within the subarachnoid space and they will produce a sharply defined rounded defect in the Pantopaque shadow. They are eccentric in at least one projection and, if large enough, displace the cord to one side. In such cases the subarachnoid space is wider than normal above and below the tumor (figure 4). Below the level of T12 to L1, the cord has terminated and the canal contains only the cauda equina. In this re-

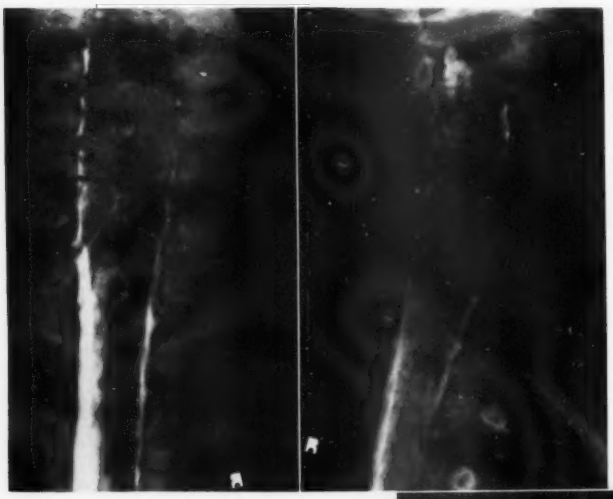

FIGURE 3. Frontal and lateral views of large intramedullary glioma, with diffuse enlargement of the spinal cord from C1 to C7 simulating syringomyelia.

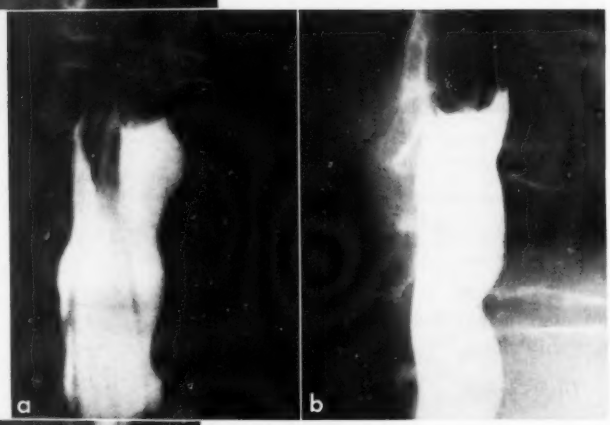

FIGURE 4. a. Frontal view of an intradural extramedullary tumor (meningioma). This view was made with the patient's head down and shows displacement of the cord laterally and widening of the dural canal just below the tumor.

b. Lateral view, showing apparent intramedullary location. An intramedullary tumor cannot be ruled out with this view only.

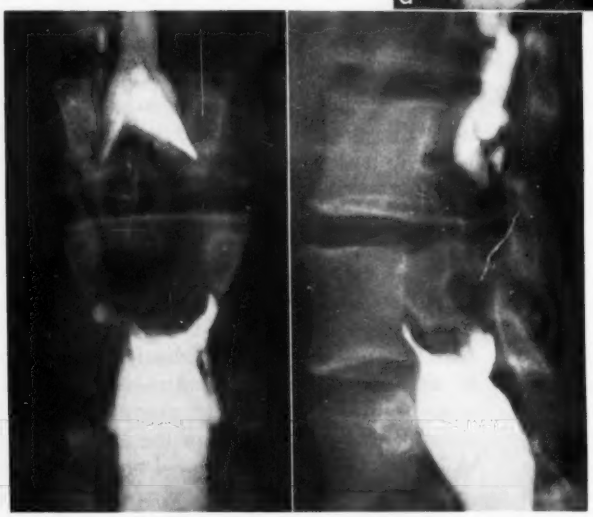

FIGURE 5. Frontal and lateral views of extradural dermoid in the region of the cauda equina, showing typical defect with widening of the dural sac. Erosion of the posterior borders of several vertebrae is seen.

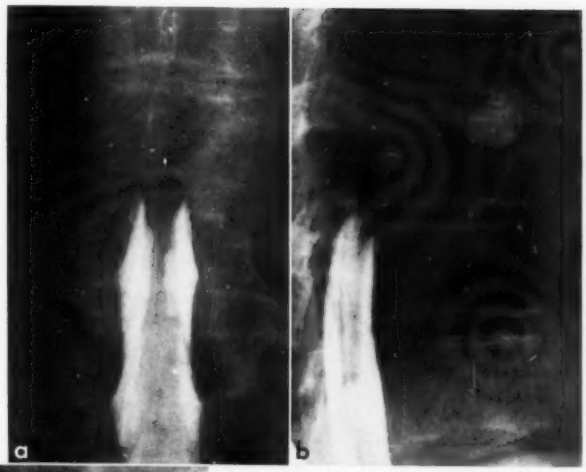

FIGURE 6. a. Frontal view of extradural tumor (metastatic carcinoma of the prostate). In this view, the lesion is indistinguishable from an intradural neoplasm.

b. Lateral view, showing posterior displacement of the dural canal and spinal cord, with narrowing of the subarachnoid space at the level of the tumor.

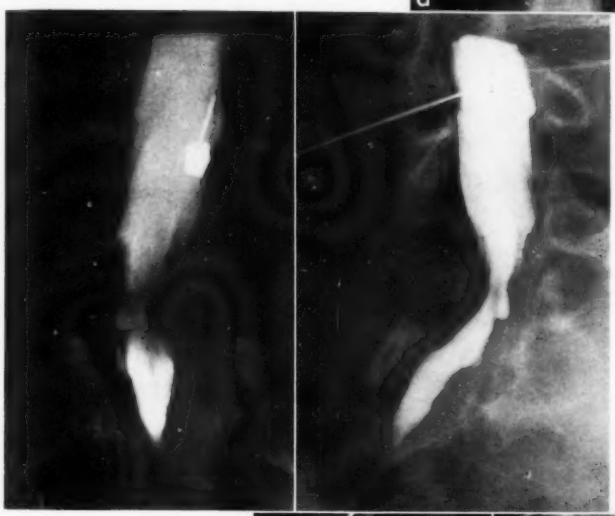

FIGURE 7. Frontal and oblique views of an extradural hemangioma. The entire canal, including nerve-root sleeves, is displaced laterally and anteriorly in the lumbosacral region.

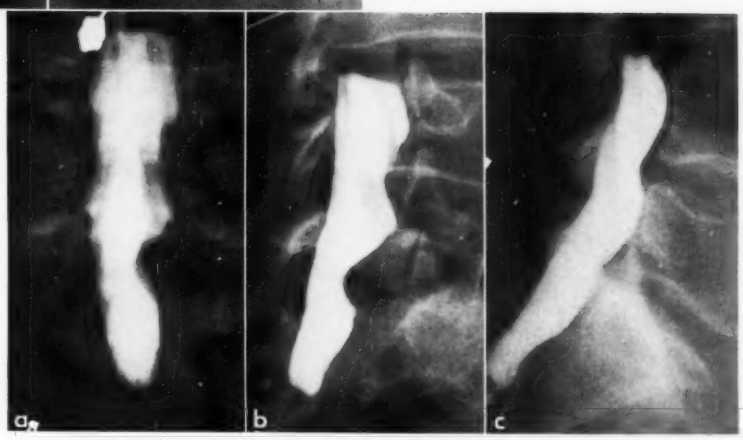

FIGURE 8. a. Frontal view of a moderate anterolateral protrusion of an intervertebral disk (L5-S1).

b. Right oblique view, showing maximal encroachment on the canal.

c. Lateral view, showing minimal encroachment on the canal.

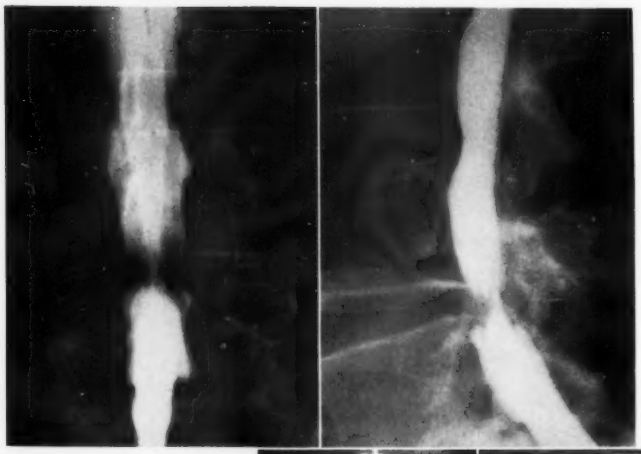

FIGURE 9. Frontal and lateral views of gross anterolateral protrusion of an intervertebral disk (L4-L5). Particularly in the frontal view, the protrusion appears to be bilateral, but there was surgical proof that it was present only on the left side (see text).

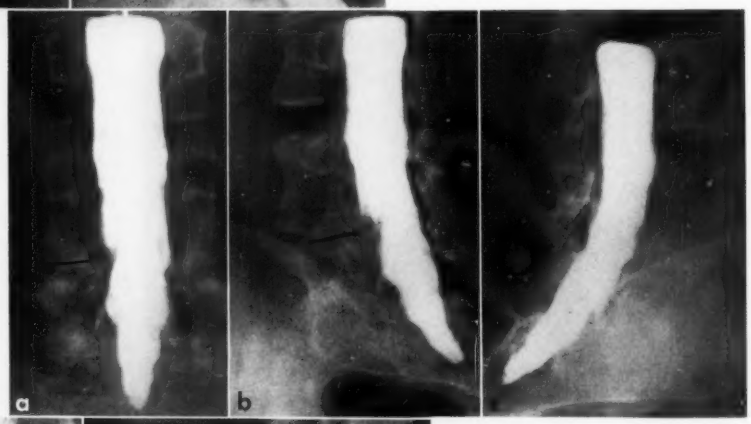

FIGURE 10. a. Frontal view of small disk protrusion amputating nerve-root sleeve (L5-S1, right side). The arrow indicates the amputated sleeve.

b. Right oblique view, showing amputation more clearly.

c. Left oblique view, showing no indentation.

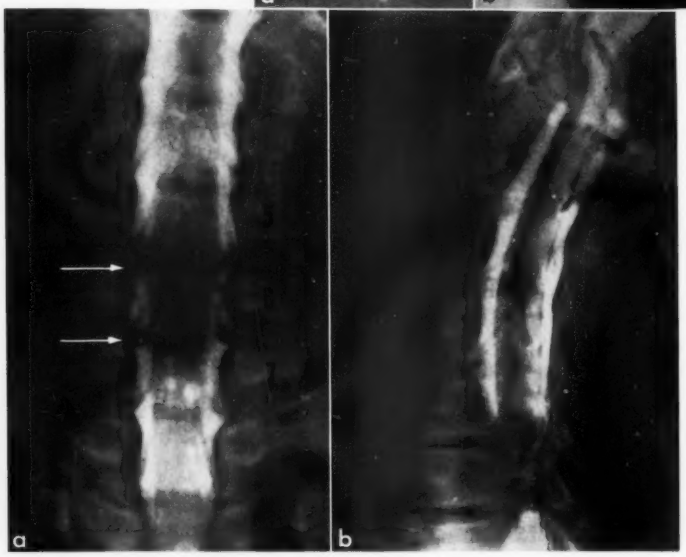

FIGURE 11. a. Frontal view of a midline protrusion of two cervical disks (C5-C6 and C6-C7). Radiolucent bandlike defects are seen at the disk levels.

b. Lateral view, showing anterior compression of the spinal canal at the same level.

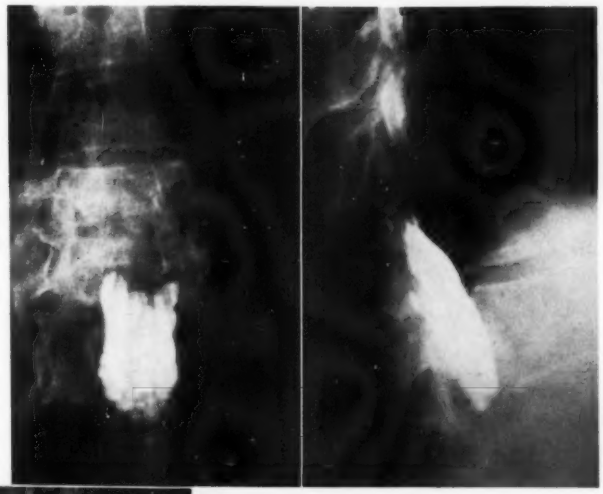

FIGURE 12. Frontal and lateral views of tuberculous abscess of the spine (T10-T11). There is extradural compression of the canal and destruction of the cartilage space between the two vertebral bodies.

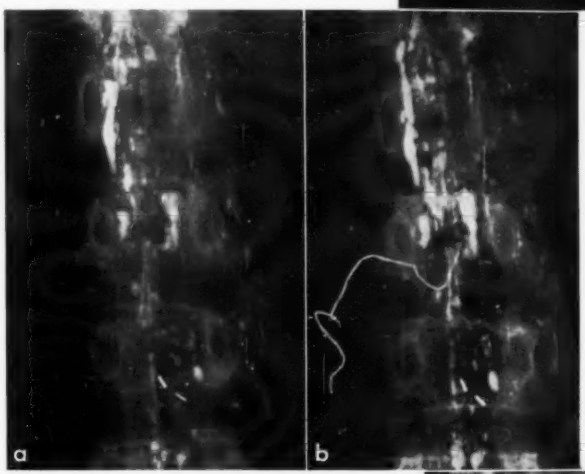

FIGURE 13. a and b. Roentgenographic appearance of arachnoiditis. The Pantopaque is collected in small cavities and does not move with a change of the patient's position. Surgery for the protruded disk was performed about one year before this examination.

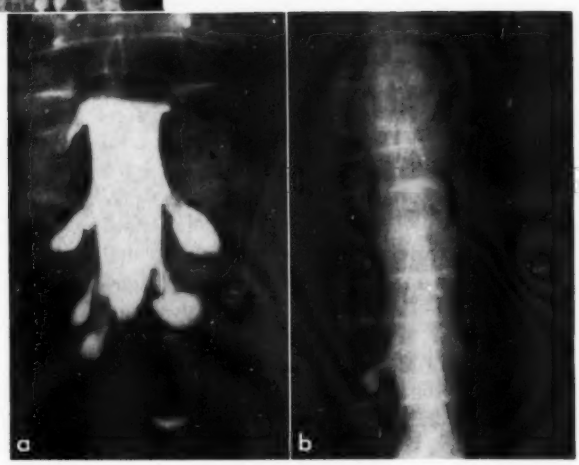

FIGURE 14. Normal nerve-root pouches in the lumbar (a) and thoracic (b) regions. The presence of large nerve-root pouches is without clinical significance.

gion, myelograms serve only to distinguish between masses in the subarachnoid space and those which are extradural (figure 5).

Most of the tumors of the subarachnoid space are neurofibromas and meningiomas. Less frequently, one sees sarcomas, extramedullary hemangiomas and metastatic neoplasms. Chordomas and dermoids are relatively rare. About 4 per cent of all subarachnoid tumors are multiple.

Extradural Tumors

These tumors displace the subarachnoid space and, if large enough, the spinal cord and often obliterate one or more nerve sleeves (figures 6 and 7).

Metastatic or primary tumors of the epidural tissue and of the vertebrae, abscesses, vascular malformations, distended epidural veins, and epidural hematomas following traumatic lumbar puncture produce similar changes.

The most commonly encountered extradural lesion is the posterior protrusion of an intervertebral disk. Typically, it occurs in the cervical and lumbar spine, and in approximately 14 per cent of cases there are multiple protrusions. In many cases regular roentgenograms of the spine show a narrowing of the involved disk space, but the demonstration of a normal intervertebral disk space does not exclude a protrusion. In the lumbosacral spine a protrusion usually is in the anterolateral portion of the spinal canal, where it produces sharply defined unilateral indentation of the dural sac, with the narrowing seen best in one of the oblique projections (figure 8).

Occasionally, there are bilateral protrusions of the same disk, but in most cases a bilateral deformity of the dural canal is caused by a large unilateral protrusion. Such a large protrusion of disk material displaces the dural sac into the posterior angle of the spinal canal and brings it in close contact with the ligamentum flavum, which covers the posterior wall of the spinal canal. This ligament is often hypertrophied in disk diseases and compresses both sides of the dural sac, simulating bilateral disk protrusion (figure 9).

Lateral and small anterolateral protrusions sometimes can be diagnosed only by amputation of nerve sleeves due to edema of the nerve root (figure 10), and some lateral protrusions cause no myelographic changes.[10]

Midline protrusions in the lumbar region are rare. They may be obscured in frontal projection by the contrast material, but are easily recognized in lateral films. In the cervical spine, midline protrusions are common because of the anatomic relationships. On frontal films, they are visible only as a transverse band of decreased radiopacity (figure 11). In the past, some have attached great clinical significance to cervical disk protrusion, but the conviction is growing that many patients with demonstrable cervical disk protrusion have no symptoms referable to them.

Prolapsed disks and some tuberculous abscesses indent the Pantopaque shadow in a manner practically identical with that of extradural tumors. The fact that a particular indentation lies at the level of a disk argues against but does not rule out neoplasms (figure 12).

Other Abnormalities of the Spinal Canal

Arachnoiditis produces multiple irregular pockets in the subarachnoid space which collect small amounts of Pantopaque. Such collections do not shift with change of posture of the patient (figure 13). Arachnoiditis usually is the result of spinal surgery or inflammatory processes.

Herniation of the cerebellar tonsils through the foramen magnum (Arnold-Chiari syndrome) can be diagnosed by means of cervical myelography.[11]

Usually, the normal nerve-root pouches are small, but occasionally they are large, even in the absence of disease (figure 14). It seems probable that a condition that some have called "communicating perineural cyst" is merely an unusually large but otherwise normal nerve-root sac.

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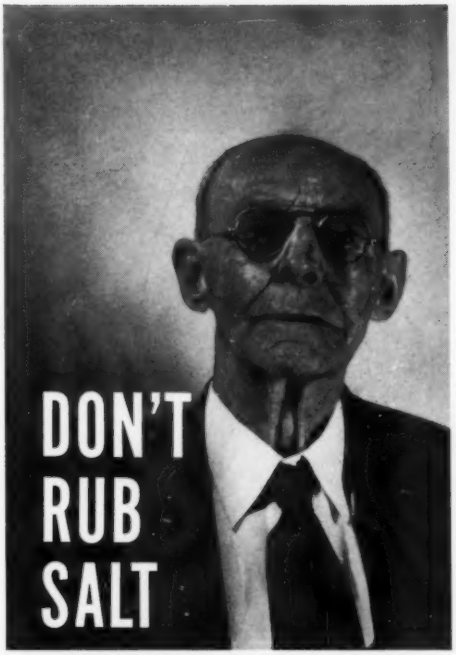

IN HIS CARDIAC WOUND

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Out of 30 intestinal antiseptics studied for preoperative bowel sterilization

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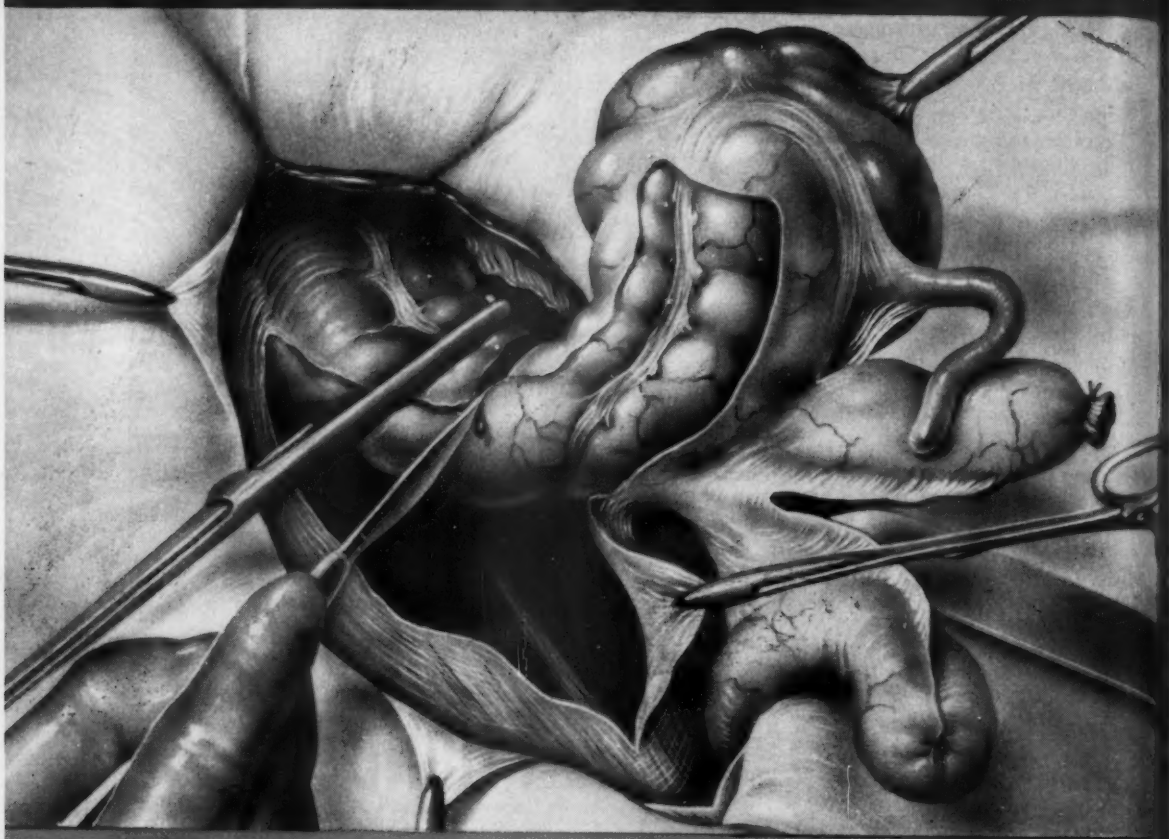

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CAPSULES

—for local effect in gastrointestinal tract; not for systemic infection

Based on their experience with 30 intestinal antiseptics for preoperative bowel sterilization, Colon and Longacre reported that oral KANTREX is "classified as a preferred drug,"[1] and can be "highly recommended for preoperative preparation of the colon."[1] Other investigators have reported that oral KANTREX is "an effective intestinal antiseptic,"[2,3] producing "excellent results."[2]

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References: 1. Cohn, I., Jr., and Longacre, A. B.: Antibiotics Annual 1958-9, p. 761. 2. Finegold, S. M., et al.: Ann. N. Y. Acad. Sci. 76:819, 1958. 3. Finegold, S. M., et al.: Antibiotics Annual 1958-9, p. 806.

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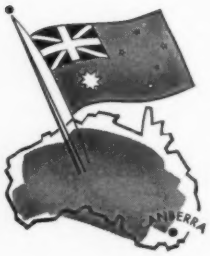
Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

AUSTRALIA



Giardia lamblia in children—During the course of an investigation into the causes of steatorrhea in a large group of infants and children, stools were routinely examined for the presence of parasites and pathogenic organisms. *G. lamblia* cysts constituted the only abnormal finding in the stools of a small number of these children, and symptoms were relieved when the parasite was eradicated. Since this investigation was conducted, other children have been studied. In the *Medical Journal of Australia,* Drs. J. M. Court and Charlotte M. Anderson, Royal Children's Hospital, Melbourne, described the clinical histories of some of these children infested with *G. lamblia.* They discussed the pathogenicity of this parasite and compared their findings with those of other workers in this field.

There is a great deal of confusion in the literature regarding the pathogenicity of *G. lamblia.* The parasite is found in the duodenum and small intestine; the trophozoites sometimes appear in large numbers in aspirates of duodenal fluid. The cysts are passed in the stools and are easily recognized.

Much of the earlier work in which various symptoms were attributed to *G. lamblia* is suspect because of lack of controls and inability to eradicate the organism. These symptoms included diarrhea or irregular bowel habits, abdominal pain, flatulence, dyspnea, inability to gain weight, anemia, nervousness, headache, dizziness and lassitude. Outbreaks of acute enteritis in children and adults also have been reported as having been caused by *G. lamblia.* On the other hand, numerous authors contend that there is no proof that *G. lamblia* causes any symptoms. However, since an effective means of eradicating the parasite has been found, more convincing evidence of pathogenicity has been available.

Giardia infestation has been regarded as a cause of failure to thrive and of weight loss in infants and young children. Careful studies have suggested that this is due to failure to absorb foodstuffs rather than to any toxic effect. Affected children may be underweight, but eradication of the parasite will produce an increase in weight.

The means by which this parasite exerts a harmful effect has been a subject of discussion. Some authors believe that the trophozoites irritate the intestinal mucosa. Signs of gastritis on gastroscopic examination of patients with *G. lamblia* have been reported. Duodenal aspirates may contain an excessive number of mucosal cells. Symptoms may be produced by the mechanical action of large numbers of the parasite which block the absorbing surface of the upper part of the small bowel. The parasite attaches itself to the intestinal mucosa by means of a large ventral sucker and, since enormous numbers of the parasite may be present in the bowel, the absorbing surface may well be reduced. No evidence of intestinal inflammation has been noted at autopsy or in specimens of duodenal aspiration, but cells from the upper part of the small bowel frequently have been found to be distorted in these specimens; this has been at-

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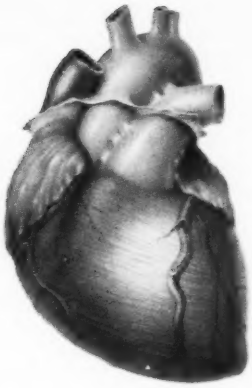
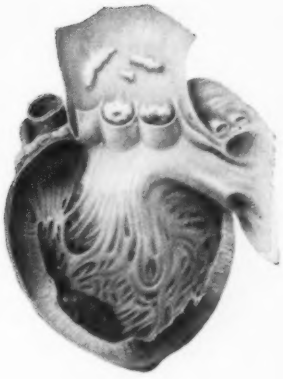


IN ANGINA PECTORIS AND CORONARY INSUFFICIENCY

. . . the treatment must go further than vasodilation alone. It should also control the patient's ever-present anxiety about his condition, since anxiety itself may bring on further attacks.



AFTER MYOCARDIAL INFARCTION

. . . it is frequently not enough to boost blood flow through arterial offshoots and establish new circulation. The disabling fear and anxiety that invariably accompany the condition must be reduced, or the patient may become a chronic invalid.

Protects your coronary patient better than vasodilation alone

Unless the coronary patient's ever-present anxiety about his condition can be controlled, it can easily induce an anginal attack or, in cases of myocardial infarction, considerably delay recovery.

This is why Miltrate gives better protection for the heart than vasodilation alone in coronary insufficiency, angina pectoris and postmyocardial infarction. Miltrate contains not only PETN (pentaerythritol tetranitrate), acknowledged as basic therapy for long-acting vasodilation. What is more important — Miltrate provides Miltown, a tranquilizer of *proven* effectiveness in relieving anxieties, fear and day-to-day tension in over 600 clinical studies.

Thus, your patient's cardiac reserve is protected against his fear and concern about his condition...and his operative arteries are dilated to enhance myocardial blood supply.

Supplied: Bottles of 50 tablets. Each tablet contains 200 mg. Miltown and 10 mg. pentaerythritol tetranitrate.
Dosage: 1 or 2 tablets q.i.d. *before meals* and at bedtime, according to individual requirements.

REFERENCES

1. Ellis, L. B. *et al.:* Circulation *17*:945, May 1958. **2.** Friedlander, H. S.: Am. J. Cardiol. *1*:395, Mar. 1958. **3.** Riseman, J. E. F.: New England J. Med. *261*:1017, Nov. 12, 1959. **4.** Russek, H. I. *et al.:* Circulation *12*:169, Aug. 1955. **5.** Russek, H. I.: Am. J. Cardiol. *3*:547, April 1959. **6.** Tortora, A. R.: Delaware M. J. *30*:298, Oct. 1958. **7.** Waldman, S. and Pelner, L.: Am. Pract. & Digest Treat. *8*:1075, July 1957.

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tributed to the mechanical effect of the trophozoites' ventral suckers.

In the cases presented in this study, it would have been difficult to prove that *G. lamblia* played the major role in causing the symptoms. In a few cases an associated factor, such as parental neglect, may well have been partially responsible. There was more definite evidence of the pathogenicity of *G. lamblia* in those cases in which steatorrhea was demonstrated and in which normal fat absorption followed eradication of the parasite, with no other treatment being given. Treatment consisted of administering 100 mg. mepacrine hydrochloride B.P. per day for five days. If the cysts did not disappear completely from the stools, a second course was sometimes necessary.

BRAZIL

Epilepsy—A brief and up-to-date appraisal of the clinical and medicolegal aspects of epilepsy by A. A. Guimarães and A. Moura has been published in *Boletim do centro de estudos do hospital dos servidores do estado.* The authors recommended that epileptics should be grouped according to Henry Gastant's electrographic classification.

The problem of rehabilitating the epileptic following hospitalization was discussed. The various approaches considered were based on whether or not the patient had permanent mental disturbances. It was proposed that a special medical committee be formed to evaluate the capacity of the epileptic for public service.

Polyposis of the stomach—M. R. Oliveira, P. Bove and P. D. Branco have presented a discussion on diffuse polyposis of the stomach in *Revista do Hospital das clínicas da Faculdade de medicina da Universidade de São Paulo.* They covered the history, incidence, etiopathogenesis, pathology, symptomatology, diagnosis and treatment of this condition. They also described two individual cases in detail, documenting their observations with x-rays and photographs. Preoperatively, malignancy was suspected in both of these cases, but it was not confirmed by pathologic examination.

The following conclusions were drawn:

1. Gastric polyposis occurs rarely; however, there is a high incidence of atrophic gastritis with gastric polyposis, seeming to indicate an etiopathogenic relationship between these conditions.

2. Malignant degeneration in diffuse gastric polyposis has been demonstrated by clinical and experimental studies.

3. The polymorphic symptomatology of gastric polyposis necessitates tests such as radiologic examination, gastroscopy, and cytologic examination of the gastric lavage for confirmation of diagnosis.

4. Since gastric polyposis is a precancerous lesion, partial, subtotal or total gastric resection should be performed. The extent of the resection depends on the localization of polyps.

Obstetric prognosis after cesarean section—Because of the increased number of women undergoing cesarean sections, J. O. Araujo, N. A. Pedral Sampaio and J. A. Pinotti have studied 228 cases from the Obstetric Clinic of the University of São Paulo to determine the prognosis in future pregnancies in these women. They have reported the following conclusions in *Anais brasileiros de ginecologia:*

1. There is an apparent decrease in the parity of patients who have cesarean sections.

2. The method employed in previous deliveries (cesarean section or transvaginal delivery) does not affect the parity of the patients.

3. Functional dystocia increases in pregnancies following cesarean section; it becomes more marked after repeated cesarean sections.

4. Retention of the placenta occurs more frequently in patients who previously have had cesarean sections than in those who have had normal deliveries.

5. When considering the method to be used during the confinement of a patient who has had a cesarean section in the past, particular attention must be paid to the location of the previous incision.

6. The fact that a pelvic disorder necessitated one cesarean section does not imply that a second one will be necessary.

7. Some authorities recommend a maximal time of 8, 9 or 10 hours of labor before transvaginal delivery should be performed in a patient who already has had a cesarean section. In the cases studied by the authors the average duration of labor preceding the first transvaginal delivery after a cesarean section was 13 hours and 11

(Continued on page A-90)

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minutes, which made the former finding seem illogical.

8. The expression "Once a cesarean, always a cesarean" is not accurate. Each case should be carefully considered in regard to a possible transvaginal delivery in future pregnancies. However, since the percentage of stillborn babies, rupture of the uterus, and maternal mortality is greater in transvaginal deliveries after previous cesarean sections, the physician should perform another cesarean section in questionable cases.

ENGLAND

Infections of the eye—Infections of the interior of the eye are grave emergencies and call for immediate and expert treatment. Relatively uncommon, they are seen after intraocular operations or perforating injuries or in severe infections of the cornea. In contrast, infections of the outer eye occur daily. When the infection is bacterial in origin, treatment with antibiotics is generally efficacious, but viral infections still are a considerable problem.

Professor Arnold Sorsby, London, has pointed out in the *British Medical Journal* that the poor penetration of many antibiotics into the interior of the eye greatly limits the value of systemic administration of these drugs in treating intraocular infections. Fortunately, subconjunctival injection of some antibiotics is a feasible procedure in expert hands and gives excellent results. For external infections of the eye, local application is so eminently satisfactory and so readily given that neither systemic administration nor subconjunctival injections often are necessary.

Penicillin, streptomycin, chloramphenicol and the tetracyclines are widely used systemically, and all are valuable as local applications in ophthalmology. The extensive use of penicillin ointment as a prophylactic measure after removal of corneal foreign bodies and after other minor injuries to the eye has greatly reduced the incidence of infected corneal ulcers and mucopurulent conjunctivitis. Ointments of penicillin, chloramphenicol or the tetracyclines are commonly used in treating subacute and acute conjunctivitis and blepharitis, replacing almost entirely all the older remedies.

With regard to antibiotics for local administration only, Professor Sorsby stated that the outstanding agent in this group is neomycin. It has an exceptionally wide range of action against bacteria, including penicillin-resistant *Staphylococcus pyogenes* var. *aureus* and many Gram-negative bacilli, among them many strains of *Pseudomonas pyocyanea.* It is not particularly effective against *Diplococcus pneumoniae,* but in the concentrations applied locally this limitation is not apparent.

Treatment of acute ear inflammation—In a discussion at the Royal Society of Medicine, Dr. T. A. A. Hunter, Marlborough, said that since the war as medical officer of a large boarding school he has treated between 20 and 30 cases of acute otitis media annually. In only one patient has there been a failure of resolution in the presuppurative phase, and that patient had come from another school. As a school doctor, he sees his patients as early as or even earlier than the general practitioner and can treat them with nursing assistance under hospital conditions, so there is no difficulty in administering injections.

Dr. Hunter's routine treatment for otitis media is the immediate administration of 1½ megunits of DURACILLIN® intramuscularly, followed by 2 capsules of penicillin V every four hours, missing night doses, until the eardrum is normal. It is most exceptional for this to take more than two or three days. Admittedly, this is a large dosage, but it produces results. Dr. Hunter suggested that much of the criticism that has been leveled at penicillin is due to an insufficient initial dose and the failure to maintain a constant effective blood level for a sufficient period. Although in theory orally administered penicillin can be effective, in practice it is likely to produce both these errors. He declared himself undeterred by the bogy of penicillin sensitivity. It is a rare condition, and the risk of its occurrence is infinitely less than the risks of serious complications in otitis media untreated by antibiotics.

Corticosteroids in skin diseases—Hydrocortisone or its analogs have been applied locally for the treatment of virtually every skin condition known, whether it be congenital, traumatic, inflammatory, allergic, metabolic, infectious, degenerative or neoplastic. However, Dr. C. D. Calnan, the London dermatologist, has emphasized in the *Practitioner* that the only processes for which these agents can be reliably recommended are eczema, dermatitis, anogenital pruri-

(Continued on page A-92)

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tus and perhaps facial and flexural psoriasis. Topically applied steroids have three very strong points in their favor: supreme cosmetic acceptability, powerful antipruritic qualities, and an almost complete absence of both side effects and drug resistance. As a consequence, hydrocortisone may appear to be a panacea for any dermatosis, especially if the latter is accompanied by itching, when no other specific medication is known. It allows the physician too readily to forget the old dictum that diagnosis precedes treatment. The antipruritic effect of hydrocortisone is second only to that of anesthetics; its mechanism is uncertain, but presumably must be related to the reduction of inflammatory changes, in spite of the fact that the latter may be minimal or absent in many patients with anogenital pruritus who respond successfully to treatment.

It cannot be overemphasized that these drugs are merely suppressive and not curative. On each occasion that a patient using topically applied steroids returns for review, the physician should consider what is being achieved and what he hopes to achieve, and ask himself whether a repetition of the prescription is justified in relation to any or all of its three principal values. Steroid ointments, creams and lotions do not smell or stain or soil clothing; they can be prescribed in a greasy or vanishing-type base as desired. It is understandable that patients prefer them to many of the alternative dermatologic preparations, which may be colored or messy or soil their clothing with grease or by leaving a dry powder. Patients will at times be well satisfied just by the relief of itching induced by the steroid application, irrespective of whether or not the morphologic aspects of the lesion are altered.

FINLAND

Myocardial infarction—Data on 683 cases of myocardial infarction have been reported by Dr. Teppo Vartio in *Annales medicinae internae Fenniae.* The patients included 519 men and 164 women; the average age was 57 years, 55.2 years in men and 63.6 years in women. The ratio of men to women was 3.2:1; in patients more than 65 years of age it was 1.2:1, and in the age group from 46 to 65 years it was 3.7:1. In the group less than 41 years of age, all the patients were men.

The number of patients hospitalized with myocardial infarction rose from 10 in 1946 to 105 in 1958, an increase of from 0.19 to 0.95 per cent of the total number of hospitalized patients.

The highest incidence of myocardial infarctions was during the months of December, January and February. Attacks occurred most frequently on Saturday and Monday, with the majority occurring at midnight or shortly afterward. The next greatest incidence was observed in patients at work during the day, especially in those involved in light manual work. A detailed inquiry failed to reveal a high prevalence of occupational stress in patients less than 41 years of age.

The primary mortality was 26.3 per cent; in men the rate was 27.1 per cent and in women it was 23.7 per cent. Mortality increased with advanced age. It was suggested that the five year prognosis in myocardial infarction in patients less than 41 years old was slightly better than in older patients. A little better capacity for work also was observed in the younger age group.

Acoustic neurinoma—Laitinen and Pakarinen have reported observations on 104 cases of acoustic neurinoma treated in the neurosurgical department of the Finnish Red Cross Hospital. Eighty-three per cent of the patients were women, averaging 42 years of age. The first subjective symptoms were hypacusia, vertigo and tinnitus of approximately two years' duration. The most usual neurologic findings included corneal anesthesia in 82 per cent of the cases, ataxia in 64 per cent, positive Romberg sign in 50 per cent, facial paresis in 49 per cent, dysmetria in 33 per cent, dysdiadochokinesia in 31 per cent, deviation of the tongue in 25 per cent, palsy of the sixth cranial nerve in 14 per cent, and pharyngoparesis in 11 per cent. Papilledema was found in 30 per cent. Four patients had normal hearing on the side of the tumor. Caloric response was considered normal in 16 per cent who were examined otologically.

Occurrence of rabies—Although the incidence of rabies in Finland during the past 30 years has not been high, it did increase following World War II, according to Rislakki's report in *Duodecim.* Cases of rabies were observed, as usual, close to the southeastern border, which is inhabited on both sides, but also includes large forest tracts and wilderness where foxes and a

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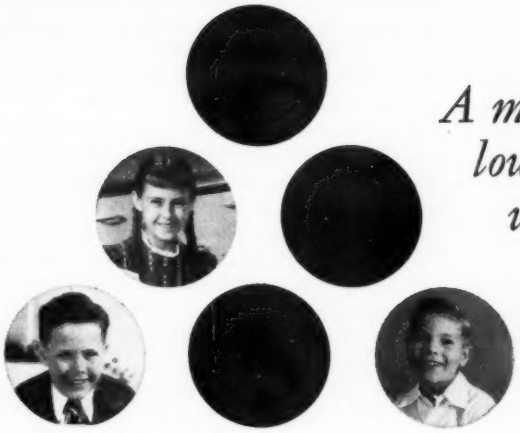

A moderate low-fat well-balanced breakfast for children 10-12 years of age

It has been found that those who develop obesity in childhood appear to have more of a dietary problem than those who develop obesity in the adult years. As a service to those advising about the obese child, a basic cereal and milk breakfast is worth consideration. *Its fat content of 10.9 gm. provides 20 per cent of the total calories, thus it is moderately low in fat.* It is well-balanced as shown in the chart below. The Iowa Breakfast Studies demonstrated that children of about this age have better grades and attitudes at school when they eat a *well-balanced* basic cereal and milk breakfast each morning.

Recommended Daily Dietary Allowances and the Nutritional Contribution of a Basic Cereal and Milk Moderate Low-Fat Breakfast*

Menu: Orange Juice—4 oz.;
Cereal, dry weight—1 oz.;
Whole Milk—4 oz.; Sugar—1 teaspoon;
Toast (white, enriched)—2 slices;
Butter—5 gm. (about 1 teaspoon);
Nonfat Milk—8 oz.

Nutrients	Calories	Protein	Calcium	Iron	Vitamin A	Thiamine	Riboflavin	Niacin equiv.	Ascorbic Acid
Totals supplied by Basic Breakfast	503	20.9 gm.	0.532 gm.	2.7 mg.	588 I.U.	0.46 mg.	0.80 mg.	7.36 mg.	65.5 mg.
Recommended Dietary Allowances—Children, 10 to 12 Years (36 kg.—79 lb.)	2500	70 gm.	1.2 gm.	12 mg.	4500 I.U.	1.3 mg.	1.8 mg.	17 mg.	75 mg.
Percentage Contributed by Basic Breakfast	20.1%	29.8%	44.3%	22.5%	13.1%	35.4%	44.4%	43.3%	87.3%

Cereal Institute, Inc.: Breakfast Source Book. Chicago: Cereal Institute, Inc., 1959.
Food & Nutrition Bd.: Recommended Dietary Allowances, Revised 1958. Natl. Acad. Sci.—Natl. Research Council Publication 589, 1958.
Watt, B. K., and Merrill, A. L.: Composition of Foods—Raw, Processed, Prepared. U.S.D.A. Agriculture Handbook No. 8, 1950.

**The allowance levels are intended to cover individual variations among most normal persons as they live in the United States under usual environmental stresses. Calorie allowances apply to individuals usually engaged in moderate physical activity. For office workers or others in sedentary occupations they are excessive. Adjustments must be made for variations in body size, age, physical activity, and environmental temperature.*

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few wolves are found. It is probable, therefore, that rabies is maintained in the wild animals. The disease has been diagnosed in both foxes and wolves in this region of Finland and the Union of Soviet Socialist Republics.

In addition to the police proceedings required by the Infectious Diseases in Animals Act, dogs have been vaccinated in the danger areas. The strain used in the production of Finnish antirabies vaccine is Pasteur's original virus fixé strain of 1884. The vaccine is prepared from calf brain tissue which it contains in the proportion of 1:10; its phenol content is 0.4 per cent, and it is inactivated at 37° C. Immunizing properties have proved effective (Habel's mouse test) and the vaccine has not caused paralysis. Annual vaccinations of dogs in the danger area will be continued.

FRANCE

Treatment of eczema —Statistical studies on the numerous and inconsistent treatments presently used for eczema have been published by M. Bolgert and M. Le Sourd, C. Huriez and C. Jamain, and P. Rimbaud and F. Duntze. Bolgert and Le Sourd stated that in one-third of their cases the disease was far advanced because of ineffective therapy. Most dermatologists, including Rimbaud and Huriez, use modern medications in treating eczema; others condemn the modern remedies unless they are absolutely necessary.

Most arguments concern the energetic methods of treatment; these are not used in either localized or slight attacks of eczema. Generally, patients with localized sensitization are cured without using drastic methods; energetic treatment is employed whenever eczema is widespread or is resistant to other forms of therapy. If the true cause of the disease cannot be determined, energetic treatment may be necessary even in cases of local origin.

Local treatment consists of applying slightly antiseptic, soothing medicaments; applications are reduced as the condition improves. Of the antibiotics used to treat eczema, penicillin is the most effective and produces the most rapid improvement. Huriez recommends six injections daily of crystalline penicillin, with an initial dose of 50,000 units. The tetracycline preparations are effective, but use of various forms of erythromycin has resulted in failure in many cases. AUREOMYCIN® is the best antibiotic to administer to infants.

Seventeen per cent of the patients who receive penicillin injections exhibit skin sensitization. Allergic reactions are seen less frequently when antibiotics other than penicillin are used; they occur in only 5 per cent of the patients treated with tetracycline. Erythromycin causes the least number of digestive disturbances. Regardless of the agent used, the dosage is moderate; treatment is continued for at least 10 days and frequently longer.

Cortisone therapy is begun a few days after antibiotic therapy has been initiated and the skin infection has been somewhat reduced. Rimbaud recommends the simultaneous administration of cortisone preparations and antibiotics for a few days. All the authors favor the use of deltacortisone in a maximal daily dosage of 30 mg., rarely 40 mg. They reduce the dosage by 5 mg. every five or six days, with a maintenance dosage of 5 to 10 mg. per day for a long period. Huriez stated that he had had excellent results with the decadrols, but because he found them dangerous to the suprarenal glands he now uses CORTANCYL®.

Best results of treatment are obtained and continue after the allergen has been suppressed in cases of local sensitization. Rimbaud believes that the therapeutic effect of antibiotics consists of neutralizing the secretion of hyaluronidase, which is produced by at least 90 per cent of the bacteria and is the main cause of spread.

Atopic or constitutional dermatitis almost always recurs. Treatment must be repeated and protracted; there is no complete cure. Seborrheic eczema presents the most difficult therapeutic problem. Eczema in infants and young children requires a relatively large amount of medication (much more than in adults), and recurrences are extremely likely.

Huriez stated that he prescribes cortisonelike remedies a short time before corticotherapy is to be discontinued, when the patient is receiving only a very weak maintenance dosage. He gives salicylates to young children; for older children and adults, he uses 15 mg. of vitamin D_2 weekly for three or four months. He has proved that this method stimulates the suprarenal cortex and helps to prevent recurrences.

Huriez restricts the use of corticoid creams to treatment of small areas of eczema; such therapy

s begun immediately after antisepsis is completed and general antibiotic therapy has been initiated. Many patients are cured within two or three weeks. In eczema of this type, most of the redness should subside in less than five days to warrant continuation of the treatment. If these measures are not effective, general corticotherapy becomes necessary.

According to Huriez, the therapy described is also indicated in alopecia areata. For this condition, he gives weekly injections of hydrocortisone *in situ*, supplemented by large doses of vitamin D_2. In cases of extensive spread he employs general corticotherapy with vitamin D_2.

These reports were abstracted from the *Bulletin de la Société française de dermatologie et de syphiligraphie* and from *La semaine des hôpitaux de Paris.*

GREECE

Greek Dermatological Union—At a meeting of this organization held in the Evangelismos Hospital, Dr. Alfred Marchionini, professor of dermatology and former rector of the University of Munich, Germany, reported on the relationship of dermatology to the theoretical sciences and the arts. By applying new methods based on both social and ethnologic studies, he clarified the etiology and pathogenesis of such dermatoses as noma, pellagra, acne rosacea and rhinophyma. He supplemented his lecture with verses from Goethe and Shakespeare and slides of paintings and sculpture by Ghirlandajo, Velázquez, Frans Hals and Veit Stoss.

Representing the University of California at Los Angeles School of Medicine at this meeting were Dr. Thomas H. Sternberg, professor of dermatology, and Dr. Paul Levan, associate professor of dermatology. Dr. Sternberg reported on amphotericin B and griseofulvin in fungous diseases, and Dr. Levan commented on a movie of the use of heparin in allergy.

Dr. Frederick Reiss, associate clinical professor of dermatology and syphilology, New York University School of Medicine, and secretary-general of the International Society of Tropical Dermatology, discussed recent progress in the treatment of the common types of dermatoses.

Refresher courses—The annual refresher courses in cardiology, pharmacology, pathology, rheumatology, tuberculosis, radiology, surgery, toxicology, radioisotopes, orthopedics, balneotherapy, urology and neurology were held at the King Paul Hospital. The program was organized by Professor N. Tsampoulas, head of the Clinic of Internal Medicine and dean of the University of Athens Medical School. Many medical films were shown and displays were presented by pharmaceutical companies and medical publishing houses.

University of Athens—At the annual meeting of the General Assembly of the University of Athens, Professor Eugene Fokas, department of balneotherapy, was elected rector of the University for the next academic year.

JAPAN

Minamata disease—In 1953 a strange disease appeared in the fishing villages on Minamata Bay near Minamata City in Kyushu. Initially, local physicians assumed that it was a viral encephalitis. In 1956 however the incidence of the disease (called Minamata disease) rose sharply, and a committee was organized to investigate its cause.

From 1953 through 1959, 78 cases of Minamata disease were recorded; mortality was 39.7 per cent. The disease had a wide age distribution but no infants were affected; 47 of the patients were men and 31 were women. Ninety per cent of the patients were involved in some way with the occupation of fishing. The greatest number of cases occurred between April and September, when the quantity of marine products in Minamata Bay was at its peak.

The chief symptoms of the disease were disturbances of the central nervous system. The initial symptom usually was acute or subacute tingling or numbness of the fingers or lips, which progressed to the tongue or lower extremities. Within several days or weeks, impairment of speech and gait and disturbances in hearing and vision appeared. The mood of the patients be-

(Continued on page A-98)

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came labile and some of them evidenced mental confusion. Cerebellar symptoms such as adiadochokinesis, inability to perform the finger-finger test, ataxic gait, and macrography were observed in most patients; various involuntary movements such as tremor and choreal and ballismlike movements were observed in some. Concentric narrowing of the visual field and disturbance of superficial and deep sensations were present in all patients. Eye grounds and cerebrospinal fluid were normal.

Viral and bacteriologic studies of the disease yielded negative results; however, research workers discovered a definite correlation between the occurrence of Minamata disease and the consumption of fish and shellfish. Most patients had eaten large quantities of fish which were probably not fresh, and most of them had eaten the viscera of the fish. Cats in the homes of many patients died of a strange disease characterized by marked central nervous system involvement; dogs in the same homes were not affected. Cats eat the viscera of fish but dogs do not. Following reports of these findings, people stopped eating fish caught in the Bay, and the incidence of the disease abruptly decreased.

Clinical symptoms and autopsy findings in Minamata disease were similar to those seen in cases of poisoning by methyl mercury. More than the normal amount of mercury was excreted in the urine and was found in the liver, kidneys and brain of patients with this disease. The same findings were observed in cats in which the disease was reproduced experimentally. Organic mercurial compounds appeared to play an important role in Minamata disease.

A polyvinyl resin plant on Minamata Bay which discards wastes containing mercurial compounds increased its production in 1953. Mud from the bottom of the Bay was found to contain relatively large amounts of mercury; when samples were taken from areas close to the plant, the mercury content increased. It appeared highly probable that mercurial compounds in the wastes from the polyvinyl plant had caused the outbreak of disease; however, feeding wastes from the plant to animals did not initiate the disease. It was concluded that the mercurial compounds became toxic only after they had passed through the body of a fish, the mechanism of which remains to be solved.

At present, the type of mercurial compound which causes the disease is unknown. Discrepancies in opinion exist among the research workers.

SPAIN

Removal of the pituitary gland in cancer— Dr. Perez Modrego of the National Cancer Institute presented a paper to the Medico-Surgical Academy in Madrid stating that the most effective endocrine treatment for cancer is removal of the pituitary gland. Some cancer patients, principally those with a primary or secondary tumor located in the sex organs, respond quite well to treatment with hormonal extracts. Such treatment has produced improvement but has never effected a complete cure.

Since it has been demonstrated that the pituitary gland plays a decisive role in the regulation of the glands of internal secretion, attempts have been made through both surgical procedures and radiotherapy to destroy the pituitary gland in order to cure a tumor located in the prostate, the uterus, the breast or other sex organs. The surgical procedure is difficult because the pituitary gland is located approximately in the center of the base of the cranium, above the sphenoid bone, and surrounded by delicate brain structures. The use of external radiation involves the danger of creating lesions in the nerve structures surrounding the pituitary gland, since these structures are more sensitive to radiation than is the gland itself.

Direct application of various radioactive substances has been used in an attempt to destroy the pituitary gland; the materials used include sponges moistened in colloidal gold or chromic colloidal phosphate, grains of radioactive gold, and screws of radiothallium. Recently, radioactive yttrium was used. Dr. Modrego employs an image magnifier, a substance applicator and the radioactive material, either gold or yttrium. The operation takes only 10 minutes and, if it were not for the effects of the anesthesia, the patient could walk out of the operating room.

During the latter half of 1959, this type of radiotherapy was employed for cancers of the breast, prostate and testicles and for all types of tumors of the pituitary gland. Dr. Modrego selected patients with advanced cancer of the genital organs which had metastasized and which had not responded to surgical or medical treatment. To date, only the most insignificant complications have been encountered.

Bedside Cardiac Diagnosis

(ARE HISTORY, PHYSICAL EXAMINATION AND CLINICAL JUDGMENT OUTMODED?)

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While the newest technics for diagnosing cardiac conditions are valuable and should certainly not be omitted when indicated, the traditional bedside skills should still be developed and used.

A thorough history, inspection, palpation and auscultation, roentgenogram of the thorax, and electrocardiogram should provide a definite diagnosis in a high proportion of cases.

Overlying all technics and procedures is the element of judgment, which comes from experience and a logical interpretation of available information.

In the last scientific session of the American Heart Association there was a symposium on new developments in supplementary diagnostic technics, with papers on left heart catheterization, indicator-dilution technics, and cineangiocardiography given by E. Braunwald, E. H. Wood and F. M. Sones, Jr., respectively. The fourth paper was given by me and contained the material presented herein; to give balance to the symposium, the program chairman, Dr. McKusick, believed someone should speak for the clinician and his bedside skills.

The weaknesses of man†

Originally the assigned title for this dissertation was, "What is new in cardiac diagnosis at the bedside?" The answer to *this* question is "Confidence." By "confidence" I mean

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Read at the 1959 meeting of the American Heart Association at Philadelphia, Pennsylvania.

†Reproduction of a photograph by the author of the lowest panel of a column, of Chartres Cathedral, which portrays the weaknesses of man. This carving, implying "Pride goeth before a fall," seems especially appropriate to the potentiality of an error in diagnosis and epitomizes the Hippocratic aphorism of experience being fallacious and judgment difficult, or the Galenic interpretation of experiment being dangerous and decision difficult.

a sense of security in judging when the bedside diagnosis is accurate and when special investigations are needed to establish it. Despite the increased accuracy of bedside diagnosis, it may not be good enough if a surgical procedure is in the offing, even if one's estimate of the accuracy is as high as 95 per cent. As part of the information available at the usual bedside consultation I include that afforded by the posteroanterior roentgenogram of the thorax and the electrocardiogram. Emphasis needs to be placed on the importance of gathering and integrating the data in an orderly manner. In completing the diagnostic picture, which may be likened to working a jigsaw puzzle, one should go only so far as to see the definite outline, without having a conflicting piece and without necessarily having to fill in the minor details.

History

One would expect general accord in accepting the history as important, but because it may be tedious, there may be the tendency to reduce unduly the time spent on it. In problems relating to the nature of chest pain in particular, the history is nearly all-important, but it must be admitted that the accuracy of the clinician's appraisal of the state of the coronary vessels leaves much to be desired.

It will be recognized that it is important to elicit or note the time of appearance of various signs and symptoms, such as murmur or murmurs, cyanosis, cardiac pain and shortness of breath. It may be rewarding to analyze with care the nature of past illnesses, particularly as manifestations of rheumatic fever or bacterial endocarditis. Inquiry as to traumatic episodes and assessment of the nature of dramatic changes of sudden nature may give the clue to the diagnosis; for instance, rupture of an aortic sinus aneurysm.

The familial history of cardiac disease may be the outstanding feature of some problem cases, not only in the familial myocardiopathies but also in some gross structural congenital defects as well. Occasionally, to observe the repetition of a rare cardiac defect, as if from the same template, is an amazing experience. In our collection of congenitally deformed hearts, there was one heart with a very rare defect, a hypoplastic right ventricle and a congenital tricuspid stenosis; this year, five years later, another child, interestingly of the opposite sex, born to the same parents, died and the heart was found to be an exact replica of the other. The clinical picture was like tricuspid atresia, but because of the previous familial event the correct diagnosis was suggested.

Approach to the Examination

Physical examination using the traditional approaches of inspection, palpation and auscultation, together with a roentgenogram of the thorax and an electrocardiogram, should allow the diagnosis to be made definitely more often than not. It may be noted that percussion is eliminated from our bedside methodology—it may be entertaining, but as a practical way of getting anywhere diagnostically it is just as outmoded ("obsolete") as a 1904 automobile. I could, but will not, orient this communication toward bedside diagnostic triumphs or bedside diagnostic humiliations, or, by selected cases, illustrate where special complicated procedures were unnecessarily done or where, in other cases, special investigations should have been carried out.

I should like to point out an uncommon error of a limited diagnosis. Of a group of difficult problems associated with congenital cardiac defects which were studied clinically *and* by cardiac catheterization and which, months or years later, were analyzed at postmortem examination in the Mayo Clinic, about a third were found to be incompletely diagnosed. These were not simple cases and probably our diagnostic acumen has increased in the past 10 years. As examples of incompleteness, the following may be cited: the diagnosis of aortic incompetence without aortic coarctation being recognized in the background, the diagnosis of rupture of an aortic sinus aneurysm without a ventricular septal defect being recognized, the diagnosis of a ventricular septal defect without the evidence of a patent ductus arteriosus or associated mitral insufficiency being recognized, and the diagnosis of aortic valvular disease in a patient having angina

but without associated coronary sclerosis being recognized.

In the approach to the patient, one aims to take the history and do the physical examination in an orderly manner. However, one may perchance have been asked previously to review the roentgenogram of the thorax, the electrocardiogram, the phonocardiogram and even the catheterization data or angiocardiographic films. I would submit that it is as great a challenge to approach the patient from this direction, knowing these data, and to attempt to vindicate their worth or otherwise; or perhaps, even at such a late phase in the investigation of the patient, unabashedly to suggest on the basis of clinical data a different diagnosis from the one that has been arrived at on the basis of laboratory data. The one approach is no less scientific than the other as long as preknowledge leads not to any prejudgment (prejudice).

Inspection

At the very onset of the examination, even before the patient is seen, his voice may suggest the diagnosis; for instance, a characteristic hoarseness may suggest myxedema. The general appearance is important: Witness the plethora of polycythemia, the ragged fingernails of hyperthyroidism. Dr. Kepler, a deceased colleague, used to say that if the doctor had not diagnosed an endocrine disorder before the patient had taken off his coat, he probably would not diagnose it at all. When the patient is undressing, one's ears may pick up evidence of dyspnea. All too often, I fear, the cardiac consultant does not observe the patient in some type of exercise in the office setting, relying perhaps entirely on the story given by the patient or the parents. In the ambulatory patient the duration of postexercise distress may often be a more important indication of the disability than the immediate discomfort. The individual's general habitus, nutrition and muscular development will be apparent, including any chest deformity such as prominence of the precordium in some youngsters with a congenitally enlarged heart. One would recognize the Marfan stature in the older child and adult, but the possibility of the Marfan trait manifested only by pulmonary artery or aortic dilatation would be kept in mind.

Differential cyanosis is rarely encountered but is diagnostically helpful when present, as in an infant that has transposition of the great vessels and patent ductus with the hands being more cyanotic than the feet, or in the opposite situation in which there is patent ductus with reversal of flow. In rare cases of the latter condition there may be a recognizable difference between the two hands as well as between the hands and the feet. One way to demonstrate such a difference is to have the patient elevate both arms with the fists clenched, then lower them to a dependent position, and open the hands, and then to observe the flush of blood entering the palms, the right hand being a brighter red than the left.

Venous pulse in the neck—I should like to dwell at some length on the venous pulse in the neck, long claimed as the particular and traditional province of the cardiologist. The visual measurement of increased mean venous pressure is remarkably accurate. This ready clinical assessment of venous hypertension seems not infrequently overlooked; for instance, in cases of constrictive pericarditis masquerading as portal cirrhosis. The early rapid diastolic drop in pressure in the distended cervical veins associated with constrictive pericarditis is a reliable but not pathognomonic sign of this condition. Only rarely is there an express need of actually measuring the venous pressure with a manometer, notably in making special comparative or long-term studies.

Perhaps relatively new in general recognition and application among practitioners is an improved differentiation of the traditional positive and negative jugular pulse waves. For example, the strong presystolic (atrial systolic) pulse in the neck, long known to be a particularly helpful diagnostic sign in patients with tricuspid stenosis, is now utilized as a strongly supportive sign of severe pulmonary stenosis and intact ventricular septum. Two diagnostic aids in this clinical area may be offered: The first is to look for the deep jugular pulse, not in the supraclavicular space, but rather at the angle of the jaw, and the second is to differen-

FIGURE 1. The arrow indicates the area below the angle of the jaw anterior to the sternocleidomastoid muscle where deep jugular pulsation usually may be seen best in the supine patient. The tongue blade is illustrated as a straight-edge to exert pressure to obliterate the venous pulse and differentiate it from the arterial pulse.

The distention of the external jugular is incidental in the illustration, as is the fact that the subject had Ebstein's malformation of the tricuspid valve and did show a prominent atrial venous wave.

tiate a venous pulse from an arterial one by moderate pressure of a straightedge above the clavicle (figure 1). Positive pulsations in the external jugular are rarely as important or useful as in the deep jugular, but the reverse may be true of the negative waves. An atrial systolic-pressure wave may be seen also in cases of pulmonary hypertension of various causes, though of lesser magnitude than in the foregoing diagnoses.

The presystolic pulsation, or so-called giant A wave, also may occur in patients with rare types of obstruction to the flow of blood to the left side of the heart, as in a patient with tricuspid atresia and a minute foramen ovale. For example, an infant with tricuspid atresia had had a Potts type of aortopulmonary anastomosis carried out, and after a few months succumbed from heart failure. There was a strong hepatic pulse, which my colleague, Dr. Ongley, suspected was presystolic, and a recording showed that it was (figure 2). The right atrial systolic pressure was high, at 25 mm. of Hg, actually the equivalent of the normal right ventricular systolic pressure.

Parenthetically, for teaching purposes I can recommend the film on the jugular venous pulse made by Dr. Paul Wood under sponsorship of the Wellcome Laboratories.

Palpation

In palpation of the thorax and of the carotid and femoral pulses I find considerable enjoyment in, but will not often commit myself to, an absolute prediction regarding the hemodynamic state or the absolute and relative sizes of the two ventricles. It is most valuable in one's clinical appraisal to note whether the heart is hyperactive or not, and to assess the characteristics of the pulsations over the left side of the thorax; for example, the heaving impulse of a large left ventricle, low in the axilla, can be readily differentiated from the diffuse precordial lift of a volume-overloaded right ventricle, or from the very sharp ill-sustained thrust in the left upper parasternal intercostal spaces that often obtains in severe pulmonary or right ventricular hypertension. In some instances of mitral insufficiency or aortic insufficiency or both, a double apical thrust in each cycle, related sequentially to systole of the left ventricle and diastolic rapid-volume overloading, may be perceived (figure 3). Sometimes one can certify the presence of severe elevations of pulmonary arterial pressure more confidently from appraisal of the force of the palpable vibration associated with closure of the pulmonary valve than from the degree of loudness of the second sound in the pulmonary area.

The importance of recognizing thrills is not to be underrated. However, it should be mentioned that one of the previously regarded infallible signs of classic mitral stenosis, namely, a diastolic thrill at the apex, can no longer be considered infallible. This thrill may occur

FIGURE 2. Phonocardiogram with electrocardiogram and hepatic-pulse recording respectively, to illustrate the last item in particular, with the marked presystolic (atrial systolic) pulse. Right atrial pressure at venous catheterization was 25/10, with a giant A wave. Left atrial pressure at arterial catheterization was 12/5. See text for discussion. The patient had tricuspid atresia, with a Potts aortopulmonary anastomosis done at seven months of age and with death occurring at 11 months of age.

with a relative mitral narrowing, with gross mitral insufficiency being the only significant structural lesion. When mitral incompetence and stenosis coexist, with calcification of the valve, systolic and diastolic thrills are not uncommonly felt.

A collapsing or Corrigan pulse is usually an incidental detail in an examination revealing the diagnosis of aortic incompetence (or undue "aortic runoff"). However, in an occasional infant who superficially presents the picture of a ventricular septal defect, with a hyperactive heart, a systolic murmur, and left ventricular hypertrophy (or volume overloading) revealed in the electrocardiogram, the collapsing femoral pulse may be the first clue to the fact that one is actually dealing with a large patent ductus arteriosus.

Auscultation

The old world of auscultation, revisited, may appear a new world for exploration. More scientific maps of it now exist, made possible by studies of the correlation of auscultatory phenomena with the hemodynamic and anatomic states. What one used to hypothesize about can now usually be related to known physiologic events and structural abnormalities. A recommended reference in the auscultatory domain is the Goulstonian Lectures by Leatham.[1] Knowledge has advanced to the point of allowing descriptive short cuts in terminology but, useful as such terms may be in day-to-day practice, one wonders whether abbreviations or colloquialisms such as "flow," "ejection" and "diamond-shaped" murmurs as recorded in an institution's permanent records will be intelligible in the years to come.

Avoidance of auscultatory error and oversight—With apologies to the many who might be affronted by the simplicity of a presentation on eradicating auscultatory error and oversight, I shall list some important items.

1. One must listen, with specific objectives in mind, in order to hear. One should listen over large areas of the body—scars, etc.

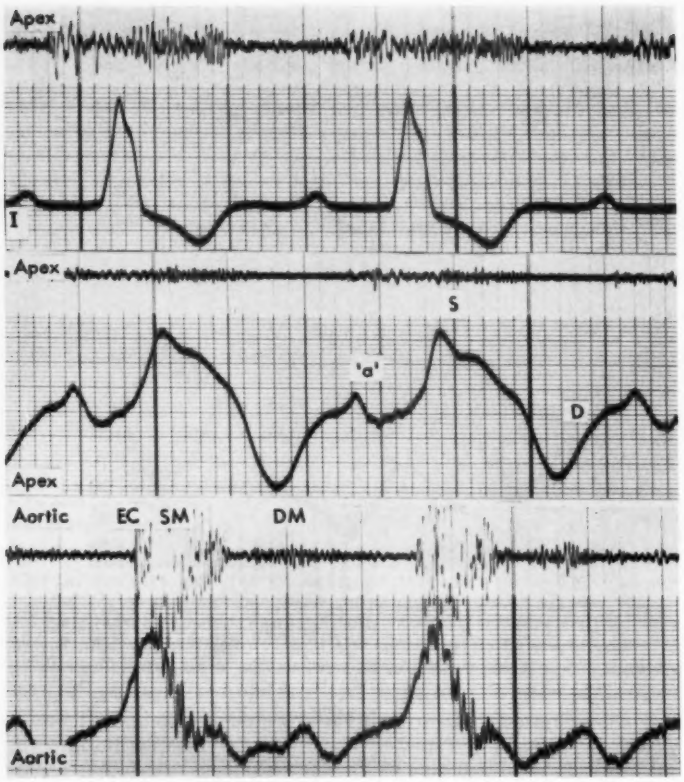

FIGURE 3. Records from a man 50 years old with aortic stenosis and insufficiency and marked poststenotic dilatation of the aorta. Of particular note is the apex cardiogram illustrating the systolic (S) and diastolic (D) thrusts and the minute thrust (a) related to ventricular distention by atrial systole. The last could not be appreciated by palpation.

In the lower panel are recorded the phonocardiogram and the pulsation over the aneurysmal dilatation of the ascending aorta. EC, ejection click; SM, systolic murmur; and DM, diastolic murmur.

2. Favorable environment must pertain.

3. One must know how systole and diastole are ordinarily identified; in a rapid heart, this is not always as simple as it seems.

4. One must recognize the tendency of "spill-over" in interpretations; for instance, if one hears a loud split second sound, there is the tendency to call the split more marked or widened than it actually is, or to call a loud murmur a long one.

5. One must test one's skill at times against a visual counterpart of the sounds produced. For instance, with practice, one can usually gauge a split second sound to 0.02 second.

6. One must use adequate equipment for the occasion, and it scarcely needs repetition that the bell stethoscope may be a necessity if one is to hear the low-frequency rumble in some cases of mitral stenosis. A number of combination bell and diaphragm stethoscopes are available, but short connecting tubes, for example, 10 in., may be too short for comfort, and to hear well one has to be comfortable.

7. Experience must guide and not rule. Knowledge of the anatomic and physiologic conditions that are possibly consistent with the varied clinical signs will alert one to various diagnoses. One must avoid allowing experience to be an absolute dictator. For instance, to say, "I have never heard a tricuspid murmur as loud as that," may lead to error, as actually it may well be the first time that it has been experienced. It may also lead to error to declare, "That is a loud pulmonary second sound," when actually the area where the loud second sound is heard, and where it is automatically and erroneously related to pulmonary-valve closure, overlies the aorta and aortic valve because transposition of the vessel is present (figures 4 and 5).

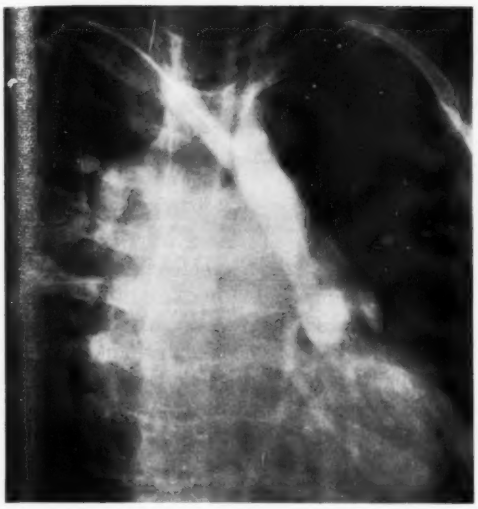

FIGURE 4. Aortogram in a case of "corrected transposition" of the great vessels. The aorta being also anterior, it can readily be appreciated that a loud second sound being heard in the "pulmonary area" could lead the examiner to the erroneous conclusion that pulmonary hypertension is present.

Incidentally, the right coronary artery having the mirror pattern of the usual left coronary may be seen. The patient was 20 years of age and had severe pulmonary hypertension and a ventricular septal defect.

FIGURE 5. Selective angiocardiogram in a case of situs inversus, "corrected transposition" of the great vessels and valvular pulmonary stenosis, which was made 1.4 seconds after an injection of 30 ml. of 90 per cent HYPAQUE®. The loud second sound suggested pulmonary hypertension, and the pulmonary stenotic murmur was central and less intense than is usual with patients who have severe pulmonary stenosis. The reader may be helped in his orientation by viewing the illustration in a mirror.

The patient was 31 years old. The pressure was 160/0 mm. of mercury in the right ventricle and 125/75 in the radial artery, and a small right-to-left shunt was present through a foramen ovale.

Clinicians in decades past ascribed a "tambour" quality to the aortic second sound with aortic dilatation; this may be a real diagnostic aid and I hope there are no scoffers among my readers.

Inadequately used auscultatory phenomena—In wondering about which auscultatory phenomena are perhaps inadequately utilized in diagnosis, I prepared a list and submit it here for critical appraisal (table 1). In each instance I can say that on occasion I have not utilized to the fullest advantage the signs herein mentioned.

Accentuated first sound—Sharply accentuated first sounds are still a strong clue to the presence of mitral stenosis. Occasionally, however, in patients with mitral insufficiency, and particularly in types related to apparent enlargement of the mitral ring or ruptured chordae tendineae, one may hear a sharp accentuated first sound.

Splitting of second sound—Wide splitting of the second sound, unaffected by the respiratory cycle, is now an established sign strongly indicative of an atrial septal defect with a high pulmonary flow. In a patient with roentgenologic evidence of a high pulmonary flow, perhaps with a fairly loud, left parasternal murmur and a second sound that is only narrowly split, one should suspect that the condition is *not* atrial septal defect but rather a condition in which there is near equalization of the pressures in the two ventricles, namely, a ventricular septal defect. If the condition is a ventricular septal defect, the cardiac silhouette in the roentgenogram and the electrocardiographic findings should help in indicating some left ventricular enlargement. In rare instances of ventricular septal defect, however, I have heard splitting of the second sound that measured up to 0.05 second. In the presence

TABLE 1

AUSCULTATORY PHENOMENA INADEQUATELY USED IN DIAGNOSIS

1. Accentuation of the first sound in mitral stenosis and certain types of mitral insufficiency.
2. Wide fixed splitting of the second sound in atrial septal defect and some cases of pulmonary stenosis.
3. Paradoxical splitting of the second sound in left bundle branch block and in left ventricular disease.
4. Single second sound in truncus arteriosus.
5. Opening snap in mitral stenosis.
6. Ejection click in pulmonary stenosis.
7. Atriogenic sounds in pulmonary stenosis and Ebstein's disease.
8. Effect of respiration on tricuspid murmurs.
9. Diastolic murmurs of the flow type—tricuspid and atrial septal defect and mitral and ventricular septal defect.
10. Importance of duration of the murmur, as well as its intensity, as in pulmonary stenosis with and without ventricular septal defect.
11. Importance of the location of the murmur, as in mitral insufficiency or ventricular septal defect with emptying into the right atrium.

of clinically distinct pulmonary hypertension and mild cyanosis, there is reason for insecurity, in some cases, in deciding whether the shunt is at the atrial, the ventricular or the ductus level or represents some combination of the three possibilities. In an occasional normal patient, in a patient with idiopathic pulmonary hypertension or with hyperdynamic circulation such as that due to systemic arteriovenous fistula, and in patients with mitral insufficiency, fairly wide unexplained splitting of the second sound may be heard.

In some instances of severe pulmonary stenosis the extent of splitting may be increased up to 0.14 second, but the problem in many of these cases is that closure of the pulmonary valve is associated with a vibration of such low intensity that the sound is muted and perhaps not heard. In addition, the systolic murmur may progress past the aortic sound, obscuring it and thus giving one no guidepost for measuring the split. As an example, a man 30 years old had been carried on the records for many years with the diagnosis of ventricular septal defect. Catheterization by the venous sampling method with the dye technic demonstrated a small ventricular septal defect with a left-to-right shunt of between 10 and 15 per cent; in addition, however, there was an infundibular pulmonic stenosis with a pressure gradient of approximately 50 mm. of mercury across the stenotic site. If one could have heard or identified the delayed pulmonary second sound (figure 6), this diagnosis would have certainly been more evident.

In cases of infundibular stenosis the systolic murmur tends to be of longer duration than in cases of valvular stenosis of comparable systolic gradient, but at the bedside this has not been of significant help to me diagnostically. The duration of the systolic murmur may be of real help in differentiating two categories of pulmonary stenosis, namely, that with and that without ventricular septal defect. *Without* a ventricular septal defect the murmur of pulmonary stenosis increases in intensity and duration (figure 7) in accord with the degree of severity of the stenosis. *With* a coexisting ventricular septal defect, the opposite is the case. Thus in Fallot's tetralogy, the general rule is that with increasing severity of the pulmonary stenosis the murmur becomes shorter and less intense. Vogelpoel and his associates[2] have published noteworthy data concerning clinical quantitation of these phenomena. Thus, from the viewpoint of my surgical colleagues, the child with tetralogy and a short insignificant murmur gives grave concern as to the suitability of the condition for surgical reconstruction, because of the diminutive pulmonary tract.

There always appear to be exceptions to any seemingly established rule, and such an exception was a case of severe pulmonary stenosis and *intact* ventricular septum, with heart failure in which *no* murmur could be heard.

With further regard to splitting of the second sound, it is probably now well known that in patients with left bundle branch block, one may not infrequently hear increased splitting of this sound in expiration, which suggests the diagnosis. Also in some instances of coronary disease and hypertension, without left bundle branch block, this paradoxical split may be noted. When the second sound is single and no split whatsoever can be recognized during the respiratory cycle, it may be an unusual but normal situation; however, in the child

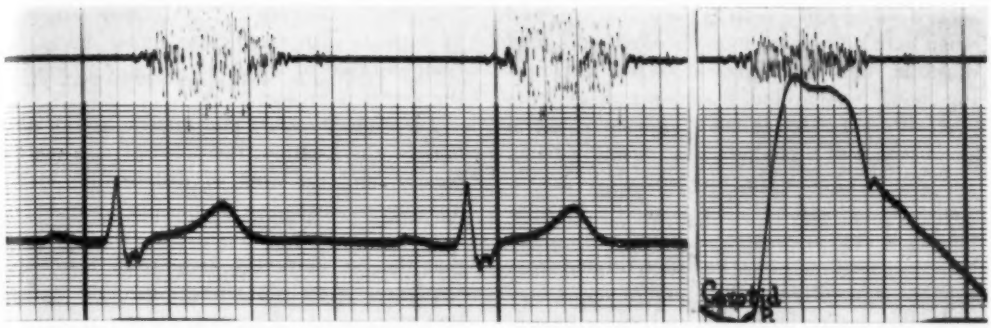

FIGURE 6. Phonocardiogram showing a muted delayed pulmonary second sound occurring in a patient with subvalvular pulmonary stenosis and a small ventricular septal defect. The duration of the murmur that encompasses the aortic second sound is also to be noted. The extent of the split second sound is 0.12 second, though the late component was not audible. See text for discussion.

The pressures at cardiac catheterization were 25/10 in the pulmonary artery, 26/4 "high" in the right ventricle, 85/3 "low" in right ventricle, and 9/3 in the right atrium.

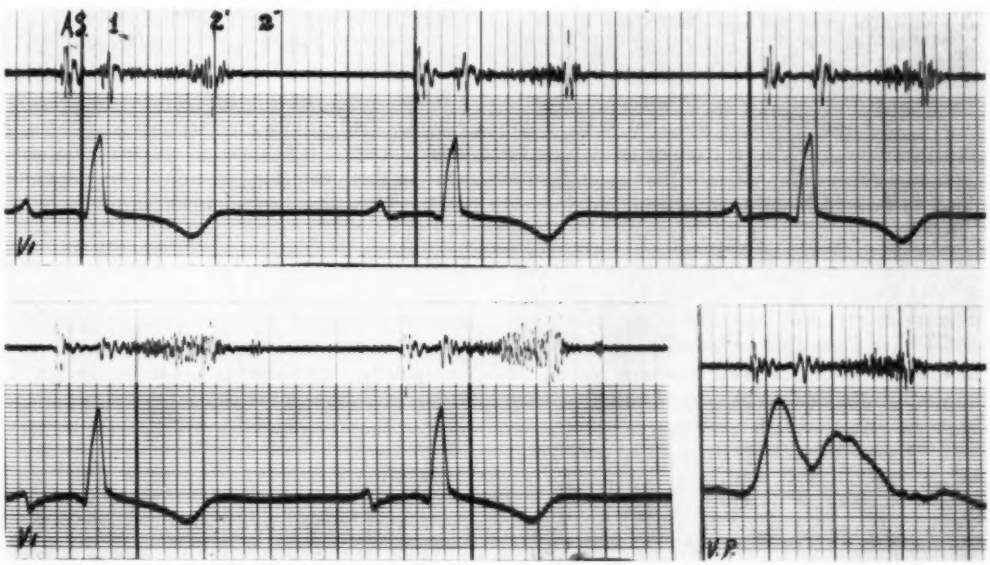

FIGURE 7. Phonocardiogram showing a prominent atriogenic (presystolic) sound, a prolonged systolic murmur ("kite-shaped"), and wide splitting of the second sound in a patient with pulmonary stenosis and intact ventricular septum. The jugular pulse represented in the lower right panel shows the prominent A wave, the peak of which does not coincide with the maximal intensity of the atriogenic sound, assumedly because of delay in the recording device.

The pressures before repair were 15/5 mm. of mercury in the pulmonary artery, 150/5 in the right ventricle, and 18/5 in the right atrium.

this finding may fit nicely into the diagnosis of truncus arteriosus, though, of course, a single second sound is often present in tetralogy with severe pulmonary stenosis.

Opening snap of mitral stenosis—I must confess that despite a 20 year interest in it, I still often have difficulty in clinically identifying the opening snap of mitral stenosis and in distinguishing it from second sounds at the apex, particularly when I cannot hear both a

second sound and a snap in the apical area and when both pulmonary hypertension and a loud diastolic rumble are present. When an opening sound is identified, it remains, as in years past, of great value in the diagnosis of mitral stenosis and of a pliable valve, at the bedside.

Ejection click—The ejection click associated with pulmonary stenosis of the valvular type is of both interest and importance, and I believe that often it may be differentiated from ejection sounds over the pulmonary artery when this artery is dilated and when pulmonary hypertension is present. The ejection click may possibly be related to inversion of the dome structure of the stenotic valve (alternatingly convex and concave) toward the pulmonary artery with systole and diastole; one impressive angiocardiographic illustration of this has been shown to me by Hay.[3]

Atriogenic sounds—The atriogenic sounds associated with pulmonary stenosis are interesting auscultatory phenomena. I refer in particular to a presystolic sound that may occur and be called a right ventricular gallop, or to an actual presystolic murmur that could be related to flow of blood through the pulmonary valve as a result of atrial contraction (figure 7). The systolic pressure in the atrium may be greater than the diastolic pressure in the pulmonary artery, and in addition my colleagues and I have been able to identify an "a" wave in the pulmonary arterial pressure record. It might be claimed as remotely possible that such an atrial systolic murmur might be related to flow through an existing minute atrial septal defect owing to the large transatrial pressure gradient, but such is not a favored explanation. In Ebstein's disease, characteristic auscultatory findings may often be present, particularly presystolic sounds, a split first sound, or a short systolic murmur. In these cases there is cadence of sounds which is well nigh diagnostic; this with a chest roentgenogram and an electrocardiogram that are characteristic may establish the diagnosis beyond question.

Diastolic murmurs of flow type—It is of interest to me now how often one hears soft diastolic murmurs related to high diastolic tricuspid flows in patients with atrial septal defects, and analogous mitral diastolic murmurs in patients with ventricular septal defects, in each instance of which no organic disease of the valves is present.

Location, intensity and distribution of murmurs—The location, the point of maximal intensity, and the area of distribution of the murmur—so-called transmission—are important, particularly in regard to the possibility that the murmur may arise from resonating structures at the point where forcible regurgitant streams are deflected.[4] This concept has been of some practical importance as it relates to diagnosis of the type of mitral incompetence that may be present. For the most part, mitral regurgitant murmurs are pansystolic (or holosystolic) and have their maximal intensity at the apex or axilla. In a patient with a ventricular septal defect one may sometimes hear a pansystolic murmur posteriorly, in the left interscapular space, and be able to differentiate it from the murmur of the ventricular septal defect and diagnose an associated mitral insufficiency. In general, one expects the murmur in this posterior location to be associated with either an incompetent short posterior mitral leaflet or an overshooting of the anterior leaflet. In contrast, an anterior murmur in the upper sternal area, perhaps in some instances suspected erroneously of being related to aortic stenosis, may be ascribed to an incompetent, overshooting posterior leaflet because of rupture of chordae tendineae, or to a defect, such as a cleft, in the anterior leaflet.

Judgment

The assigned title of this communication includes reference to a personal quality called "judgment," and in the setting of the symposium it would relate to the need and choice of special tests such as outlined in the previous papers. There is the old saw that "good judgment comes from bad judgment"; as true as this may be in both medical and surgical practice, I hope it is limited in its scope. It is better to say good judgment comes from knowledge and logic, tempered as it may be by decisions which, in later review, might be called bad judgment.

A list of areas wherein experience and per-

sagacity may operate to advantage to the physician follows. I hope I insult no one's intelligence because of the simplicity of the items listed.

Roots of good judgment—1. Knowledge of incidence and clinical manifestations of the main cardiac defects.

2. Search for and recognition of associated defects.

3. Accurate assessment of complicating conditions, such as myocardial failure; advanced pulmonary vascular disease; valvular disease, pericardial disease and calcifications; and coronary disease, for example, in association with aortic stenosis and anginal syndrome.

4. Knowledge of the varied anatomic defects giving rise to the same hemodynamic profile, and vice versa. Examples of two anatomic defects that may give rise to the same gross hemodynamic profile are a patent ductus and an aortic-pulmonary "window"; a large ventricular septal defect and a single ventricle; and a common atrium and total anomalous pulmonary venous connection.

5. Knowledge of vicarious production of usual diagnostic signs. In the area of electrocardiography, three examples may be given. (a) In a ventricular septal defect, the evidence of left ventricular hypertrophy may arise from mitral insufficiency instead of from a left-to-right shunt. (b) In a tetralogy syndrome with a surgically produced aortopulmonary shunt, the electrocardiogram may mimic that commonly seen in tricuspid atresia. (c) In an atrial septal defect, hypertension and coronary disease may vicariously result in an electrocardiographic picture ordinarily seen with atrioventricular cushion ("ostium primum") defects. In the area of auscultation, examples are all conditions giving a continuous bruit, including patent ductus, truncus, and isolated constriction of a pulmonary artery.

6. Proper fitting of symptoms to signs and to patient's objectives in coming for medical attention.

Conclusion

I would emphasize the importance of the technics presented in the previous papers of this meeting, not only in elucidation of the problem of the individual patient but also in their educational impact on the bedside clinician, giving him greater understanding of the phenomena he observes and records. It is fitting to acknowledge the stimulus that Paul Wood[5] has given to many physicians meeting the challenge of diagnostic problems at the bedside, which type of approach may be reviewed in his text. If one is to be considered wise, one must view the special tests circumspectly with the specific objectives of either offering remedial care for the individual or advancing knowledge on a broad front, including improvement in bedside diagnosis.

The question in the title given to me by Dr. McKusick, "Are history, physical examination and clinical judgment outmoded?" can, I hope, be answered "no" and my position defended. However, the question is ambiguous—the dictionary gives two definitions of "outmoded," namely "obsolete" and "unfashionable." While bedside diagnoses may be unfashionable, they are not obsolete.

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Etiology and Prevention of Infectious Hepatitis

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This is the first of a series of articles on infectious hepatitis, a disease which has become increasingly prevalent, particularly during and since World War II.

In this discussion, the authors cover the known information about the etiology and prevention of infectious hepatitis. The articles to follow will concentrate on diagnosis and treatment of the disease.

DRASTIC changes in our concept of hepatitis took place at the time of World War II, when successful transmission experiments to man were first reported. Prior to that time, as Paul[1,2] and Havens and Paul[3] have pointed out, infectious hepatitis masqueraded under various names, including "acute catarrhal jaundice," "epidemic hepatitis," and "acute yellow atrophy of the liver." Today it is viewed as a viral infection, increasingly prevalent and especially in children and young adults, characterized by destructive changes in liver cells, and accompanied occasionally by a severe illness in adults and usually by a mild one in children in whom it often passes unrecognized.

Hepatitis occurs in both sporadic and epidemic forms. In civilian populations epidemics strike institutions, summer camps and, sometimes, cities. Epidemics in military groups are common during wartime. During World War II the high incidence of infectious hepatitis and its "cousin," serum hepatitis, provided the military with one of its most serious medical problems.

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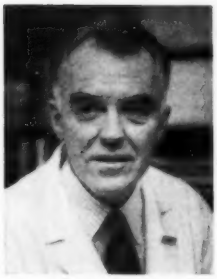
Etiology

Much of our knowledge of the causative agent or agents is derived from intensive studies using human volunteers as experimental subjects during and subsequent to World War II. Although both infectious hepatitis and serum hepatitis are believed to be caused

by viruses, no virus has been "isolated," that is to say, adapted reproducibly and unequivocally to a laboratory test object such as tissue cultures, eggs or animals. At the present time man seems to be the only susceptible host. Materials known to be capable of inducing hepatitis in man have been inoculated into a wide range of experimental animals with negative, inconsistent or unsatisfactory results. These attempts have included the use of various species of Primates, pigs, birds, embryonated hen's eggs, ducks, rats and mice. In mice and dogs, various indigenous agents, so far unrelated to the human disease, may give rise to hepatitis, which complicates the attempts to transmit human hepatitis virus to these animals. Although many laboratories have struggled to propagate hepatitis viruses in tissue cultures, only one has reported success,[4] and this has not been confirmed. It is safe to say that knowledge of hepatitis will accumulate rapidly when a practicable experimental host is found for the virus and when a specific diagnostic test, serologic or otherwise, is discovered.



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In this regard, Havens[5] has recently reported hemagglutinins for one day old chick erythrocytes in a large proportion of sera of patients in the acute stage of viral hepatitis. Tests were positive for a small percentage of normal persons and of patients with chronic hepatic disease and with other acute and chronic diseases; of special interest was the fact that none of 23 patients with obstructive jaundice had hemagglutinins. McCollum and co-workers[6] have recently described essentially similar findings.

Despite its many drawbacks, the use of human volunteers has yielded valuable information leading to the modern concepts of the natural history of infectious hepatitis. The German investigator Voegt[7] in 1942 reported the first successful transfer of infectious hepatitis (IH) virus from man to man by oral feeding of duodenal contents of a patient ill with the disease. British workers first demonstrated viremia[8] and virus in the stools.[9] The latter finding was quickly confirmed by American investigators.[10,11]

Properties of the virus—The properties of infectious hepatitis (IH) virus are compared in table 1 with those of serum hepatitis (SH) virus.

Although the size of IH virus has not been measured, it is known to pass a Seitz EK filter; it may well be small because its close relative, SH virus, is known to measure about 26 mμ.[12] IH virus appears to have great stamina; its activity is preserved in the frozen state (–20° C., –70° C.) for years. A strain we have studied was found to be infective after storage in an electric freezer at from –15° to –20°C. for two years and four months. The capacity to produce hepatitis with jaundice is not destroyed at 56°C. for 30 minutes. It has been suggested that although infectivity is not abolished, the virus titer may be reduced under these conditions; comparative titrations to determine whether or not this is true have not been made. SH virus is equally resistant, if not more so, surviving at 60°C. for four hours but becoming inactivated when heated for 10 hours at 60°C.

Both IH and SH viruses resist the action of ether, which suggests that they contain no lipid. This property, considered along with certain others, such as small size, infectivity by oral route, residence in the alimentary tract, viremia, etc., reminds one of the enteroviruses (polioviruses, Coxsackie and ECHO viruses).

Virus in the feces—Hepatitis virus has been

TABLE 1

COMPARISON OF INFECTIOUS HEPATITIS (IH) AND SERUM HEPATITIS (SH) VIRUSES AND DISEASES CAUSED BY THEM

CHARACTERISTICS	IH VIRUS	SH VIRUS
Size	Unknown; passes Seitz EK filter	About 26 mμ
Temperature resistance		
–15° to –20° C., 2 yr. 4 mo.	Remains active	Remains active
Room temperature, 6 mo.	—	Remains active
56° C., ½ hr.	Remains active	Remains active
60° C., 4 hr.	—	Remains active
60° C., 10 hr. (albumin)	—	Inactivated
Resistance to ether	Remains active	Remains active
Resistance to MERTHIOLATE®, 1:2000	—	Remains active
Resistance to chlorine, 1 p.p.m.	Remains active	—
Coagulation, settling filtration plus chlorine	Inactivated	—
Susceptible host	Man	Man
Pathologic changes	Same	

detected repeatedly in the stools of persons in the acute stages of the disease. It may be present in large concentrations, e.g., the equivalent of 0.1 gm. of stool given orally has been shown to be icterogenic.[13] Virus has also been demonstrated in stools during the incubation period two to three weeks before the emergence of jaundice[14] (figure 1). These facts fall neatly into line with epidemiologic evidence that infectious hepatitis is spread mainly by intestinal-oral pathways. Persons may be infectious before they become ill or in the absence of any practicable indication thereof.

Concerning the important question of persistence of excretion of virus after the acute phase, our knowledge is fragmentary. Capps, Bennett and Stokes[15] reported the excretion of virus in the feces of two patients with chronic hepatitis, five and 15 months after onset, respectively. Because this is the only positive report available and because others have failed to detect virus after as short a time as three weeks after the disappearance of jaundice,[16] a systematic investigation of the duration of excretion of virus following acute infectious hepatitis is needed.

Viremia—As already mentioned, Cameron[8] first reported the detection of infectious hepatitis virus in the blood in 1943. Others[11, 17, 18] have repeatedly demonstrated virus in the blood during the acute stage. Francis, Frisch and Quilligan[19] demonstrated virus in the blood three days before onset of hepatitis. Studies conducted by us[14] have also shown that viremia is present during the incubation period; in one trial it was established three to seven days, and in another two to three weeks, before onset of jaundice. Virus was not detected in a serum pool collected three to four weeks before onset of jaundice. Evidence for viremia persisting after recovery from infectious hepatitis has been hard to come by; Murray and his associates[20] demonstrated viremia in one person eight months after recovery at a time when liver function tests were normal. The question of persistent viremia, as with persistent excretion of virus in the feces, is most important from the public health standpoint and deserves further study.

It has long been suspected on epidemiologic grounds that infectious hepatitis occurs in most persons, especially in children, as a mild

TABLE 1 *(Continued)*

COMPARISON OF INFECTIOUS HEPATITIS (IH) AND SERUM HEPATITIS (SH) VIRUSES AND DISEASES CAUSED BY THEM

CHARACTERISTICS	INFECTIOUS HEPATITIS	SERUM HEPATITIS
Season	Fall, winter	Any
Age	Children and young adults	Any
Incubation period	2 to 8 weeks	8 to 26 weeks
Clinical features	Same	
Secondary cases	+	0
Virus in stools	+	0
Virus in blood	+	+
Virus transmitted orally	+	0
Virus transmitted parenterally	+	+
Homologous immunity	+	±*
Heterologous immunity	0	0
Gamma globulin suppresses jaundice	+	?

*Inconclusive; evidence indicates it is inferior to that for infectious hepatitis.

anicteric or wholly nonapparent infection. The demonstration of viremia, therefore, in a case of nonapparent infectious hepatitis was not too surprising, although it provided concrete evidence of the phenomenon: A six year old child was fed known icterogenic material and observed daily thereafter for over two months. During this period he had no fever, no symptoms, no enlargement of the liver, no jaundice, no bilirubinuria, and no abnormality of the serum bilirubin, thymol turbidity or cephalin flocculation. The only change detected in this patient was a rise in the serum glutamic oxalacetic acid transaminase with a peak value of 250 units on the thirty-seventh day. Serum obtained on this day was injected subsequently into eight persons, in six of whom hepatitis developed, with jaundice in three and without jaundice in three, after incubation periods varying from 33 to 47 days.[14] Although the stools of the child with proved nonapparent hepatitis have not been tested for virus, it would be surprising not to find it in view of results in other trials with serum and stools obtained during the incubation period (figure 1). It seems highly probable that persons with subclinical or nonapparent infection are the most efficient and dangerous spreaders of infectious hepatitis.

Incubation period—One of the differences between infectious hepatitis and serum hepatitis lies in the length of the incubation periods —relatively short (two to about eight weeks) in infectious hepatitis and longer (8 to 26 weeks) in serum hepatitis. This difference applies to both the experimentally induced and the naturally occurring examples of the disease. The incubation period in infectious hepatitis appears to be unaffected by dose of virus or portal of entry. A strain (or strains) of infectious hepatitis virus studied by us is associated with a longer incubation period (35 to 50 days) than most other strains studied experimentally.[14] Some of the incubation periods greater than 50 days, as recorded in figure 1, are probably spurious and are the result of secondary infection acquired from exposure to group mates during the incubation period when the latter were excreting the virus.

Methods of transmission—There is a large body of evidence derived from both epidemi-

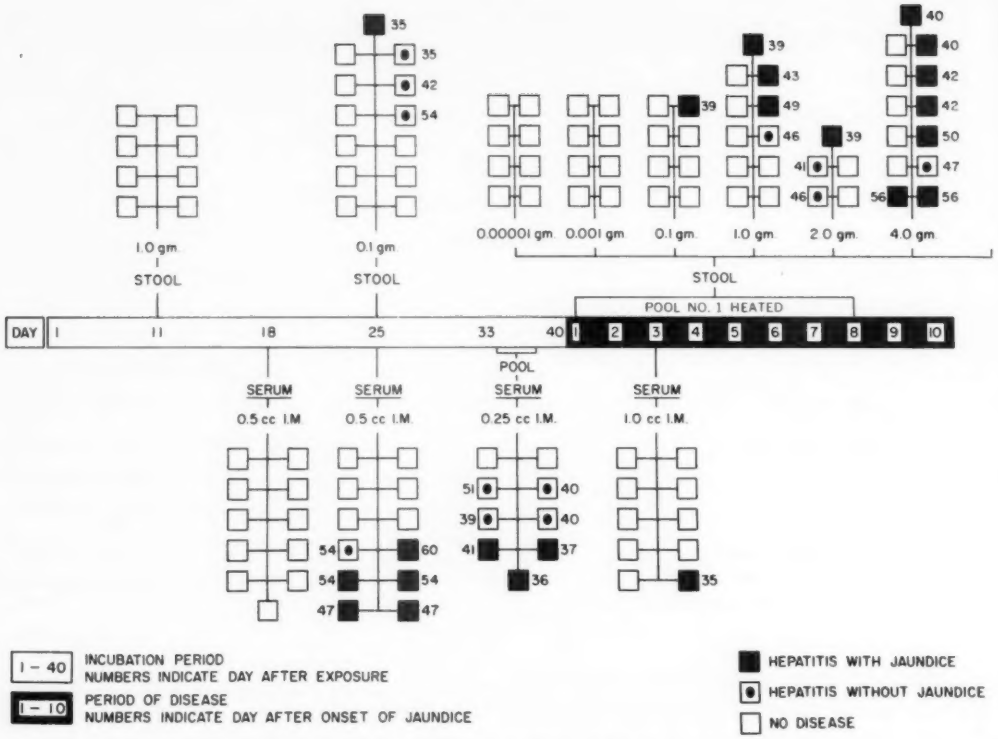

FIGURE 1. Schematic summary of studies of the period of infectivity of infectious hepatitis.

Virus was detected in stools obtained on the twenty-fifth day of the incubation period (two or three weeks before the onset of jaundice) and on the first to the eighth day of disease. Viremia was detected (1) on the twenty-fifth day of the incubation period, (2) three to seven days before the onset of jaundice, and (3) on the third day of disease.

The stools and sera collected on the eleventh and twenty-fifth days of the incubation period were obtained from three patients. Fifteen other patients contributed to the serum pool, which was collected three to seven days before the onset of jaundice. Stool pool No. 1 was prepared from stools obtained during the first eight days after onset of jaundice in six naturally infected patients. Serum was obtained from one patient on the third day after onset of jaundice.

(Reproduced with permission from: Krugman, S. and Ward, R.: Infectious Diseases of Children. Ed. 2. St. Louis, The C. V. Mosby Company, 1960.)

ologic and experimental studies, pointing to intestinal-oral pathways as the principal mode of spread of infectious hepatitis. Epidemics associated with poor sanitation have long been known to plague military camps. Although sharp water-borne, milk-borne and food-borne outbreaks have been described, it seems likely that the disease is transmitted mainly through intimate human association. It is well to remember that channels utilized in person-to-person contact may include the intestinal-oral circuit as well as "droplet" and mouth-to-mouth infection. Infectious hepatitis has been produced experimentally many times by feeding virus to human beings. Virus has been found repeatedly in the stools, as mentioned previously, of persons in the acute stages and during the incubation period.

Infectious hepatitis has also been induced experimentally by parenteral injection of virus. The demonstration of viremia before, during and after illness, as well as in a person with subclinical infection, illustrates another mode of transmission, e.g., an artificial one, like that of serum hepatitis, through the use of whole blood, plasma or other blood products, and of contaminated needles, syringes, stylets, etc.

Geographic distribution—Infectious hepatitis probably exists in all parts of the inhabited world. Epidemics have occurred in the Scandinavian countries, Iceland, England, Germany, Switzerland, the Balkans, the Mediterranean basin, the Far East, and the Americas. An explosive water-borne epidemic struck the city of Delhi, India, in the winter of 1955-1956. The total number of cases with jaundice was estimated to be about 29,000.[21]

Age distribution—The highest incidence in civilian populations usually occurs in the pediatric age group, i.e., persons under 15 years of age. Generally speaking, children comprise about 65 per cent of the cases. In a protracted smouldering outbreak in an institution for mental defectives, about 75 per cent of the cases occurred in patients under 20 years of age.[13] The high concentration of cases in the young has not received the emphasis it deserves. The disease in children is milder than in adults and often passes unrecognized. Children, consequently, may well be the chief transmitters and, epidemiologically, the most dangerous reservoir of infection. In support of this concept, Capps and co-workers[15] described the occurrence of infectious hepatitis with jaundice in a high proportion of new student nurses caring for infants and children under three years of age in an orphanage. Epidemiologic evidence indicated that hepatitis, largely unrecognized, was endemic among the infants and that they were the source of infection in the nurses. Hepatitis virus was demonstrated in the stools of two infants by transmission experiments to adult volunteers.

Sex distribution—From the available data, both sexes generally appear to be equally susceptible to infection. The incidence, however, has been reportedly higher in girls soon after menarche. Also, women beyond the menopause have a higher morbidity to chronic hepatitis and a higher mortality than do men. Among parents of the childbearing age, the attack rate is reported to be slightly higher for women than for men. This effect has been ascribed to the usually greater exposure of mothers than fathers to small children.

Seasonal distribution—Although infectious hepatitis may occur at any time of the year, in many areas there is a seasonal pattern in the annual distribution of cases. The incidence tends to be low in midsummer with a sharp rise occurring in the late summer and autumn. In the Scandinavian countries the peak has been reached in the late fall or early winter months. In the United States, however, the highest rates have occurred in the late winter and early spring months.

Prevention

Acquired immunity—One attack of infectious hepatitis is generally thought to confer protection against subsequent attacks. The immunity is probably not as solid as that afforded by measles, for example, because a history of previous attacks of jaundice is reported in from 2 to 5 per cent of patients. Evidence of this kind, however, is not reliable because the previous episode may have been due to some other agent such as serum hepatitis virus; it is clear that no cross immunity obtains between infectious hepatitis and serum hepatitis. At an institution for mental defectives in which approximately 525 cases of infectious hepatitis with jaundice were observed during a six year period, second attacks of icteric hepatitis were recognized in 21, or 4 per cent of this group.[22] Moreover, in one subject two attacks of infectious hepatitis with jaundice three months apart were induced experimentally by feeding aliquots of the same virus suspension. On the other hand, solid protection has been demonstrated in adult volunteers convalescent from experimental infectious hepatitis and challenged later with the same strain of virus.[23] Evidence of partial cross immunity between two strains of infectious hepatitis virus has also been demonstrated.

The existence of multiple immunologically distinct types of infectious hepatitis virus, similar to those occurring among the enteroviruses, might explain second attacks of the disease. This has not been studied systematically, nor will it be practicable to do so until a laboratory test object is discovered. Other possible mechanisms to explain second attacks are: (1) Following the primary infection, hepatitis virus may become dormant or latent for variable periods only to be triggered into

activity by unknown factors analogous to herpes simplex; (2) the second attack may be caused by the same virus in a dose so large as to overwhelm the resistance of the host; or (3) in persons having second attacks there may be deficient immune mechanisms. There is no concrete evidence for any of these possible causes.

The evidence that gamma globulin prepared from normal adult human sera will prevent icteric hepatitis when given during the incubation period indicates the presence of antibody with broad protective powers.

Control measures—In attempting to control the spread of hepatitis, procedures aimed at interrupting intestinal-oral pathways should be employed. As in other excremental infections, these procedures should include careful handwashing before eating or preparing meals and after evacuation of the bowels; proper sterilization of food utensils by boiling for 30 minutes or by autoclaving at 121° F. and 15 lb. pressure for 20 minutes; exclusion of potentially infected food handlers; suppression of flies; and other measures to prevent fecal contamination of food, milk and water supplies. There is evidence that the usual methods of chlorinating water cannot be relied on for inactivating hepatitis virus.

The detection of nonapparent cases or carriers by laboratory tests available today is unsatisfactory or impracticable. Recent studies establishing the presence of virus in feces and blood during the incubation period have already been described. Information is lacking concerning the persistence of viremia and excretion of virus in the stools. It seems advisable to consider patients potentially infectious for at least a week after onset of illness. It is strongly recommended that patients never serve as blood donors, even long after recovery from hepatitis. Careful attention should be given to the thorough cleansing and *heat sterilization* (boiling for 30 minutes or autoclaving at 15 lb. pressure and 121° F. for 20 minutes) of all needles and syringes used on patients with hepatitis. Disposable needles and syringes are recommended in the management of patients with hepatitis.

Gamma globulin—In 1945 the studies of Stokes and Neefe,[24] Gellis and associates,[25] and of Havens and Paul[26] clearly established the fact that gamma globulin is an effective prophylactic agent against infectious hepatitis. In the early trials the dose of gamma globulin was relatively high, ranging from 0.15 ml. to 0.08 ml. per pound of body weight. It is now apparent that doses ranging from 0.06 ml. to as little as 0.01 ml. per pound of body weight are effective when given during the incubation period as late as six days before onset of illness. Gamma globulin is injected by the intramuscular route. Passive protection from gamma globulin is believed to persist for six to eight weeks. Stokes and his associates,[27] working in institutional epidemics, reported that in three groups inoculated with gamma globulin protection persisted for as long as five, eight and nine months, respectively. Stokes postulated that as passive immunity waned, subclinical infections occurred in the inoculated groups which resulted in active immunity being superimposed on passive immunity, or, as he expressed it, *passive-active immunization*.

Results of investigations, similar to those described by Stokes and associates, that we have carried out during the past four years in an institutional outbreak of hepatitis have tended to support the hypothesis of passive-active immunization. Several controlled trials of gamma globulin have repeatedly shown a significant decrease in incidence of hepatitis *with jaundice* in the inoculated groups.[13,22] When the casual appearance of jaundice was used as the criterion of lack of protection in three trials of gamma globulin, the attack rates in the control groups were 2.5, 10 and about 30 times higher, respectively, than those for the inoculated groups. When a small group was studied intensively, however, for *anicteric* as well as for icteric hepatitis, no real difference was observed between the group inoculated with gamma globulin and the controls. During a six month period the number of cases—three with jaundice and six without—was exactly the same in the two comparable groups. The only possible difference was a slight delay in the appearance of hepatitis in those persons receiving gamma globulin.

From these studies of endemic hepatitis in an institution one must draw the conclusion that the effect of gamma globulin is to suppress the severity of hepatitis as manifested by the appearance of jaundice. With conditions providing continuous exposure to hepatitis virus, active immunity may well be planted on top of a waning passive protection. Under other conditions such as a family outbreak, where exposure is neither as heavy nor as persistent as that in a mental institution, the resultant protection would probably be just from gamma globulin, or passive immunity, and would be transient.

The dose of gamma globulin we recommend is 0.06 ml. per pound of body weight. From the experience of others, it appears that smaller amounts, such as 0.02 ml. per pound of body weight, are also effective.

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Mechanism and Treatment of Shock Following Myocardial Infarction

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Hemodynamic studies have shown that shock following myocardial infarction is caused primarily by sudden reduction in cardiac output to one-half of normal values, with unimportant changes in total blood volume. A high mortality accompanies this condition.

Treatment of heart block and ventricular tachycardia associated with shock can result in dramatic improvement. Morphine, oxygen and digitalis are considered routine treatment, and morphine alone may reverse hypotension without true cardiogenic shock. Although vasopressor agents may produce subjective improvement, in the author's experience they did not decrease the ultimate mortality.

Hypothermia and assisted circulation as therapeutic measures are currently in the experimental stage.

R. W. GUNTON

SHOCK is one of the more common emergencies encountered in medical practice. The clinical picture is quite familiar. The patient is pale, cold and cyanosed; he perspires profusely and has a weak, thready pulse, a blood pressure of 80 mm. Hg or less, and weak heart sounds. In some patients, stupor is also present. Secondary changes frequently develop, such as oliguria, acidosis and organic damage to the brain, heart and kidneys. To this clinical state the term "peripheral vascular collapse" often has been applied. This is a useful and acceptable term in a descriptive sense, but it may be misleading in suggesting an incorrect primary hemodynamic mechanism in some cases.

There are four fundamental factors in maintenance of the circulation: (1) venous return, (2) blood volume contained within the vascular bed, (3) cardiac output, and (4) peripheral resistance at the level of the precapillary arteriole. Deficit of any one of these four factors may cause the picture of shock. Only

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a decrease in peripheral resistance is true peripheral vascular collapse.

Types and Mechanisms of Shock

The first cause of decreased peripheral resistance to be considered is simple syncope. The man who faints in a line-up while waiting for an inoculation has no deficit of cardiac output or blood volume; he has a primary fall in peripheral resistance. Barbiturate poisoning or an overdose of hypotensive drugs may pharmacologically produce peripheral vascular collapse.

Decreased venous return at one time was thought to be common to many types of shock. Investigations of hemodynamic mechanisms have indicated that this is not always true, but there are certain interesting types of shock that probably are due primarily to decreased venous return. Gram-negative septicemia, the type seen following genitourinary infections, may be accompanied by shock. It has been shown that in this condition there may be increased engorgement of the abdominal viscera and actual trapping of blood, with decreased return to the heart. Use of the type of cuirass respirator which is employed in respiratory paralysis also may cause a decrease in venous return. The external pressure on the chest may result in an increased intrathoracic pressure, which in turn causes decreased venous return.

Decreased blood volume is the most common cause of most types of surgical shock. This condition occurs in hemorrhage; burns; soft-tissue trauma in which there may be as much as a liter or a liter and a half of fluid in the interstitial spaces; and fluid loss from emesis, diarrhea or intestinal obstruction.

The causes of cardiogenic shock are myocardial infarction, advanced congestive heart failure, arrhythmias (heart block and tachycardia), cardiac tamponade, and myocarditis. These are primarily cardiac in origin, implying a primary decrease in cardiac output. Of these, the most important is myocardial infarction. Shock complicates acute myocardial infarction in 15 to 20 per cent of cases, and the mortality of 80 per cent from this condition indicates that it is very serious.

Advanced congestive heart failure may occasionally present a shocklike syndrome when, in addition to evidence of pulmonary and systemic venous congestion, a fall in blood pressure occurs and perspiration, a thready pulse and oliguria are present.

Arrhythmias complicating acute myocardial infarction may of themselves produce shock. This is true of heart block because of the decreased systolic output. This is not the type of heart block seen in elderly people who, with recurring asystole, have attacks of the Stokes-Adams syndrome or syncope. It is an acute heart block with shock complicating infarction. Ventricular tachycardia, because of decreased diastolic filling, and cardiac tamponade also may cause the picture of shock.

The term "myocarditis" in reference to cardiogenic shock does not mean the specific myocarditis that may be seen in rheumatic fever or the toxic myocarditis resulting from chemotherapy, such as from emetine in the treatment of amebiasis. Neither is this type of myocarditis of that heterogeneous group of conditions with cardiac enlargement of unknown cause, the so-called cardiopathies. Myocarditis refers here to the type of viral infection which may occur in young people or follow an upper respiratory infection. In some cases the viral agent is known (Coxsackie B-5); in others it is not known. The clinical picture in these cases often is shock rather than heart failure.

It has not always been recognized that a fall in cardiac output is the primary and important hemodynamic disturbance in shock following myocardial infarction. It has been suggested that this state is compensatory to rest the heart, and there may be a true element of peripheral vascular collapse. To test this objectively, hemodynamic measurements have been made in patients following myocardial infarction and have been compared with normal levels. It should be emphasized that sometimes following infarction there may be hypotension, with systemic blood pressure of 80 mm. Hg or lower, without true shock (that is, without the cold, cyanosed, oligemic extremities, the perspiration, and the oliguria, which are such important signs of true shock). Often, these patients who have hypotension without shock will respond to relief of pain alone, and

within a few hours their blood pressure will return to normal. It is important to distinguish patients who have simple hypotension from those with true cardiogenic shock.

Hemodynamic measurements have shown that in true cardiogenic shock there is an unimportant reduction of plasma volume, an adequate or more than adequate central blood volume, and a primary decrease in cardiac output to one-half of normal values. When this decrease in cardiac output is compared with normal levels, it exceeds the degree of fall in blood pressure; this implies an increased peripheral resistance.

In patients with hypotension who are not in shock, the cardiac output is near normal, and the fall in blood pressure implies a decreased peripheral resistance. In this group of patients there actually is an important element of peripheral vascular collapse.

Treatment

Certain arrhythmias which produce shock following myocardial infarction may be treated. The most effective treatment for heart block is the intravenous administration of 0.2 mg. isopropylarterenol (ISUPREL® hydrochloride). This dose can be repeated or its effect can be maintained by use of Isuprel LINGUETS® (10 mg. every three hours). ADRENALIN® is still a useful drug to try. This agent may be given in an aqueous solution of 1:1000 strength (0.5 cc. subcutaneously) or in a 1:500 oil solution (1 cc. intramuscularly). Adrenal steroids have been tried with some degree of success.

The drug of choice in treating ventricular tachycardia is procaine amide hydrochloride (PRONESTYL® hydrochloride), which may be given intravenously in a dose of 0.5 to 2 gm. Initially, 0.5 gm. should be dissolved in 20 cc. saline or distilled water and given intravenously at a very slow rate over a period of 15 minutes; during this time the rhythm is monitored with an electrocardiograph. If this treatment is ineffective, it can be repeated slowly and carefully until a total of 2.0 gm. of the drug is given; if reversal does not occur at this time, the treatment should be abandoned.

Quinidine sulfate is an old and often effective remedy for ventricular tachycardia. The dosage recommended here is for an acute situation, not for elective reversal of atrial fibrillation to sinus rhythm. A suggested dosage schedule is 0.4 gm. taken by mouth every two hours. Quinidine sulfate is available dissolved in propylene glycol for intramuscular injection, 0.4 gm. being given every three hours. It is also available in the form of dihydroquinidine for intravenous injection; dosage is adjusted to the patient's requirements.

In treatment of shock following myocardial infarction, morphine is indicated for the relief of pain; in patients with hypotension who are not in shock, morphine alone may reverse the situation. Oxygen is probably useful and is most effective when given by mask. Digitalis also is advocated following recent myocardial infarction when it is complicated by true shock. It has been suggested that digitalis is dangerous in patients with recent coronary thrombosis, because it may increase the irritability of the myocardium and precipitate tachycardia or ventricular fibrillation. Its use is justified in this emergency by the fact that in most patients who survive the initial period of 12 to 24 hours of shock, signs of pulmonary and systemic venous congestion develop, and death may result from acute pulmonary edema. Often, shock and heart failure coexist. This is one of the emergency indications for digitalization; a convenient dosage schedule is 0.5 mg. digoxin given intramuscularly every three hours for three doses, followed by a maintenance dosage of 0.25 to 0.5 mg. daily.

Use of hypothermia for treating shock is in the experimental stage. The rationale for its use is that when body temperature is lowered by surface cooling from the normal 37° C. to 28° C., the body oxygen requirement is reduced to 25 per cent. This reduced requirement might be met by the low cardiac output in cardiogenic shock. Limited clinical experience with hypothermia has not yet yielded satisfactory results. Assisted circulation is another method of treatment still in the experimental stage. This implies some external means of supporting heart function with a pump. Experience with this method is limited, but veno-arterial perfusion (inferior vena cava to aorta)

through a groin incision may prove practical and helpful.

Vasopressor drugs have been advocated in recent years for the treatment of shock following myocardial infarction. The rationale is that these drugs will increase the peripheral resistance and raise aortic pressure so that there is better perfusion of vital organs, such as the brain and kidneys, and of the coronary arteries themselves. This will result in better function in areas of the myocardium which are adjacent to the infarcted area but are not absolutely ischemic, and the cardiac output will increase. There is also experimental evidence that in addition to their vasopressor action these drugs have a specific cardiotonic effect and increase the output of the heart.

Several vasopressor agents are currently being used. Methamphetamine hydrochloride (METHEDRINE®) is well known and is effective in intramuscularly administered doses of 15 to 30 mg. Methoxamine hydrochloride (VASOXYL® hydrochloride) may be given intramuscularly in doses of 20 to 60 mg. Metaraminol bitartrate (ARAMINE®) may be administered intramuscularly in doses of 10 to 30 mg., or it may be diluted in 500 cc. of 5 per cent dextrose in distilled water and given intravenously in a dose of 50 to 100 mg. Mephentermine (WYAMINE®) may be given in a dose of 30 mg. intramuscularly, or 60 to 120 mg. may be given by intravenous drip.

Currently, one of the most commonly used and potent vasopressor drugs is *l*-norepinephrine (LEVOPHED®). It can be given only intravenously; even then it may cause tissue slough. The usual dose is 8 to 32 mg. in 500 cc. of 5 per cent glucose in distilled water, with the rate of infusion adjusted from 10 to 30 drops per minute as required to maintain systemic pressure above 100 mm. Hg systolic. Higher concentrations may be required, but the risk of slough increases. This risk may be accepted in preference to infusion of an excessive amount of fluid, which may precipitate pulmonary edema. The best way to give Levophed is through a polyethylene catheter in an arm vein, with the catheter tip advanced at least as far as the axilla or into the inferior vena cava through the femoral vein.

Critical evaluation of treatment is necessary if we are to avoid therapeutic delusion. With high initial enthusiasm for vasopressor therapy, a clinical investigation was undertaken to test the efficacy of these drugs. Patients with shock following myocardial infarction were assigned either to routine treatment (morphine, oxygen, digitalis) or to routine treatment plus vasopressor agents. The original design of the investigation required that patients be assigned alternately to these two treatment regimens. This condition was not fulfilled due to the promptness of house physicians in administering vasopressor drugs before alternate cases were selected. If treatment with vasopressor drugs had been started it was not discontinued. In a group of 32 patients who had severe shock following myocardial infarction and who were treated with vasopressor drugs, the mortality was 78 per cent; the mortality in a group of 17 concurrently treated control patients was 76 per cent. There was no difference in the survival rate.

In this investigation, the vasopressor agents were effective in that in 80 per cent of the treated patients, the blood pressure was raised to 100 mm. Hg or higher; the patients seemed to be mentally brighter, and they began to put out urine. However, their average survival time was 21 hours, compared with 17 hours in the control group; the ultimate mortality was the same in the two groups. It may be that better perfusion of the brain, myocardium and kidneys is achieved only at the expense of decreased cardiac work produced by this artificial increase in peripheral resistance.

The survival rate achieved with vasopressor agents in this investigation was lower than that in other published studies. It should be emphasized, however, that only those patients with severe shock were included. Inclusion of patients who had hypotension without shock obviously would have improved the treatment results; however, this would have been an inaccurate measurement, because such patients usually recover without special treatment.

The treatment of severe shock following myocardial infarction remains an unsolved therapeutic problem. One might ask if it is because this condition is untreatable. Is this

the end stage of an irreversibly damaged myocardium? In some cases, this probably is true, particularly in older patients who have had multiple myocardial infarctions. It is not necessarily true in the younger patient in whom shock follows the first myocardial infarction. It is challenging to believe that shock in such patients is a temporary mechanical crisis which might be overcome with the help of skillful physicians, and that the patient may have more years of useful life.

Conclusions

Morphine alone is all that may be required for the treatment of hypotension following myocardial infarction.

Shock due to heart block or ventricular tachycardia may be reversed by treatment.

Digitalis should be given to patients in shock, even though on admission they have no evidence of systemic or pulmonary venous congestion, because as the state of shock continues evidence of true heart failure develops in many patients.

A trial of vasopressor agents is worthwhile. There is no decisive evidence that they do more harm than good.

We should look forward to the possibility of some practical method of supporting heart function by extracorporeal circulation and to some method of decreasing body oxygen requirement either physically or chemically in order to tide these patients over a critical emergency.

1960 INTERSTATE POSTGRADUATE MEDICAL ASSEMBLY

Oct. 31-Nov. 3 **Pittsburgh-Hilton Hotel** **Pittsburgh, Pa.**

Breakfast Conferences

Tuesday, November 1

1. Cerebrovascular Insufficiency, MICHAEL E. DEBAKEY, M.D., Houston
2. Management of Head Injuries, FRANK H. MAYFIELD, M.D., Cincinnati
3. Medical and Surgical Handling of the Postphlebitic Syndrome, T. T. MYERS, M.D., Rochester, Minnesota
4. The Practical Management of the Rheumatoid Arthritic, NORMAN O. ROTHERMICH, M.D., Columbus
5. Hyperparathyroidism—a Frequently Unrecognized Clinical Syndrome, STEFAN S. FAJANS, M.D., Ann Arbor
6. Gynecologic Diagnosis Via the Cul-de-sac, CURTIS J. LUND, M.D., Rochester, New York

Wednesday, November 2

1. Jaundice in the First Few Days of Life, GEORGE B. LOGAN, M.D., Rochester, Minnesota
2. The Trick Knee, JOHN S. DONALDSON, M.D., Pittsburgh
3. Advantages and Limitations of Griseofulvin Therapy, DONALD M. PILLSBURY, M.D., Philadelphia
4. Common Problems in Gynecology of Interest to the Medical Man, FRANK P. FOSTER, M.D., Boston
5. Intestinal Obstruction, LELAND S. MCKITTRICK, M.D., Boston
6. Use and Abuse of Antibiotics, R. S. GRIFFITH, M.D., Indianapolis

Because only a limited number of guests can be accommodated at the conferences, reservations should be made early. Write to Dr. E. R. Schmidt, Program Chairman, Box 1109, Madison 1, Wisconsin. List three in order of preference and enclose fee of $3.00.

Management of Acute Renal Failure

HENRY D. McINTOSH, ERNST PESCHEL,
H. VICTOR MURDAUGH AND VIRGINIA JOHNSTON*

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Acute renal failure invariably follows a physiologic insult which results primarily in injury to the uriniferous tubules. It may have a variety of causes which operate either by a direct toxic action or by producing renal ischemia.

The following factors should be considered in managing a patient with acute renal failure: fluid replacement; caloric intake; electrolyte, blood chemistry and hematologic abnormalities; infection; cardiovascular and other complications; artificial dialysis; the diuretic phase; and prognosis.

The patient's recovery depends principally on the type of initial insult, the physiologic state of the kidneys before the insult, and judicious management by the physician.

HENRY D. McINTOSH

THE syndrome of acute renal failure[1] has been referred to as the crush syndrome,[2,3] lower nephron nephrosis,[4] or acute tubular necrosis.[5] It invariably follows a physiologic insult which results primarily in injury to the uriniferous tubules.[1,6] Factors precipitating such renal dysfunction include trauma; profound hemorrhage or peripheral circulatory insufficiency from any cause, especially obstetric complications; transfusion reactions or other hemolytic processes; septicemia, nephrotoxic or hypersensitivity reactions; obstructive uropathy, and other less common reactions.[7,8]

These factors operate either by a direct toxic action on tubular cells or by producing renal ischemia. Oliver, MacDowell and Tracy[1] demonstrated that the lesions due to these two mechanisms differ markedly. The nephrotoxic necrosis is limited to that part of the nephron which is functionally concerned with handling the toxin, primarily the proximal convolution.

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As toxins are distributed by the renal circulation, most nephrons are equally involved. The basement membrane apparently is not affected in this type of lesion, nor are epithelial cells of other portions of the nephron. The second type of lesion results from focal cortical ischemia and occurs at random among the nephrons and in any part of a nephron. The basement membrane may be destroyed. If severe, this type of injury may lead to complete disruption of some of the uriniferous tubules (tubulorhexis). The nephrotoxic lesions may be accompanied by ischemic lesions due to circulatory changes resulting from the toxin.

Such injury may be followed by the suppression of urine formation. If this suppression is profound, products of catabolism will accumulate. Uremia develops and, if progressive, death may ensue. With careful management during the oliguric phase, sufficient time may be available to permit the cells to regenerate and adequate renal function to return.

If oliguria is of short duration, extrarenal azotemia due to dehydration or hypovolemia must be excluded.[9] The reduced urine flow may result merely from inadequate replacement of fluid losses with respect to volume or composition or both. If such deficiencies remain uncorrected, acute renal failure will develop.[10] If dehydration or hypovolemia appears likely, 1000 ml. of water with appropriate electrolytes should be administered intravenously over a 30 minute period while the patient is carefully observed. Measurement of the venous pressure is helpful when the diagnosis is questionable; a significant rise indicates an overloaded vascular bed. If the oliguria is due to a lack of water, salt or colloid, the urine output should increase to 20 ml. or more per hour. If flow does not increase, fluid must be rigidly restricted.

Obstructive uropathy must be ruled out. The syndrome of acute renal failure rarely is associated with prolonged complete anuria or with intermittent anuria (or oliguria) and polyuria. If obstruction of the urinary tract is suspected, it is imperative that the patency of the urethra or ureters, or both, be investigated.

Once the diagnosis of acute renal failure is established, regardless of the etiology, the following parameters of management should be considered:

1. Fluid replacement
2. Caloric intake
3. Electrolyte and blood chemistry abnormalities
   a. Hyperkalemia
   b. Hyponatremia
   c. Acidosis
   d. Hyperphosphatemia and hypersulfatemia
   e. Hypocalcemia
   f. Hypermagnesemia
4. Hematologic abnormalities
   a. Anemia
   b. Bleeding tendency
5. Infection
6. Cardiovascular complications
7. Miscellaneous complications
8. Artificial dialysis
9. Diuretic phase
10. Prognosis

Fluid Replacement

The first step in fluid replacement is to determine the total daily fluid loss from urine, stool, gastric secretions as vomitus or obtained by suction, sweat, and insensible loss. Accurate measurements of urine and gastric secretions are mandatory. Sweat and insensible loss can only be estimated. In temperate climatic conditions a 70 kg. afebrile patient will lose from 800 to 1000 ml. per day by sweat and insensible means.[9,11] This volume will be altered by extremes of temperature, hyperpnea, increased activity, and fever. Fever will increase the volume about 100 ml. per degree centigrade elevation.

Fluid replacement is accomplished by exogenous administration of water as well as by the endogenous water of oxidation. The water of oxidation results from the catabolism of fat stores and protein in the absence of an adequate caloric intake. The complete oxidation of 1 gm. of fat results in the liberation of a little more than 1 ml. of water. Rates of oxidation of endogenous fat up to 600 gm. a day in anuric patients have been reported.[12] This endogenous water is sodium-free and will dilute the total body stores of electrolytes. The vol-

ume of the water of oxidation will be increased by accelerated metabolism from any cause such as infection, endocrine dysfunction, response to injury, etc. In patients with excessive tissue destruction, such as that seen in war casualties, catabolism may be sufficient to result in detectable edema on a fluid intake of less than 500 ml. per day.[13]

The water of metabolism may only be estimated. A 70 kg. patient without obvious infection or excessive tissue destruction will form about 500 ml. per day. *This volume must be subtracted from the previously calculated replacement requirements.* The resulting volume is the amount which should maintain the existing state of hydration. In a 70 kg. patient with no major complications except acute renal insufficiency, the volume will amount to approximately 500 ml. per day or 0.3 ml. per kilogram per hour.[14] Infants and children will require approximately 0.5 to 1.0 ml. per kilogram per hour.[8]

Before fluid replacement for a 24 hour period is finally determined, the state of hydration of the patient must be carefully evaluated. If the patient is overhydrated, replacement fluid should be further restricted; if the patient is markedly dehydrated, the volume should be increased.

Such calculations are no more than approximations. They can be checked, however, by carefully weighing the patient daily. The average adult patient with acute renal insufficiency should lose about 0.3 to 0.5 kg. per day.[11,14] In the presence of increased metabolism, this loss will be greater. The loss of weight results from inadequate caloric intake, which is usually unavoidable. If no weight is lost, the total body water has been expanded.

The route of administering the fluid is debatable. Oral administration is always most desirable, but volumes of 300 to 500 ml. per day are tantalizingly small when administered *per os*. These patients are frequently anorectic and nauseated. Hypertonic solutions, when consumed orally, frequently precipitate vomiting or diarrhea. We therefore prefer to administer all fluids intravenously.

Hypertonic fluids can easily be administered through a catheter introduced percutaneously into the femoral vein and passed into the inferior vena cava.* Surgical cutdowns in these patients should be avoided if possible.

Permitting the ad lib. use of ice chips can prove dangerous. The average teaspoonful of ice chips represents 10 to 15 ml. of water. If taken hourly, ice chips can account for 240 to 300 ml. of additional fluid during 24 hours.

Caloric Intake

The caloric intake is inadequate during the period of oliguria. Gamble[15] showed that 100 gm. of carbohydrate provides a maximal protein-sparing effect during starvation. Such an intake reduces the negative nitrogen balance by 50 per cent and also prevents ketosis.

Despite Gamble's observations, most clinicians prefer to give at least 250 gm. of carbohydrate. If the fluid is administered by a catheter lying in a great vein, hypertonic glucose (up to 50 per cent) may be given. The amount which may be administered is predicated on the more imperative need to restrict fluid.

Many technics for administering fat as a source of calories have been suggested. None is completely satisfactory. Most patients have adequate endogenous fat stores which may be metabolized as a source of energy. Accordingly, there is little need to supply additional exogenous fat during the period of oliguria unless the patient is markedly malnourished.

Protein is contraindicated. Vitamins are probably not necessary unless dietary restriction exceeds one week.

Electrolyte and Blood Chemistry Abnormalities

Hyperkalemia—Administration of potassium is almost always contraindicated. Gropper[16] reported a case of acute renal failure implying that the cause was a profound potassium deficiency. It is uncertain that hypokalemia can result in acute renal failure. To the contrary, hypokalemia is characteristically associated with polyuria. From the report, it is difficult

*T 462 LNR thin wall, fitted stylet or 18G or 14G needle, Becton, Dickinson and Company, Rutherford, New Jersey; PE 50 (inside diameter 0.965 mm.) or PE 190 (inside diameter 1.70 mm.) polyethylene tubing, Clay-Adams, Inc., New York.

to rule out an acute exacerbation of glomerulonephritis as the cause of the oliguria.

Considerable caution must be exercised to avoid the unsuspected administration of potassium. We have seen one oliguric patient with marked electrocardiographic changes of hyperpotassemia who was receiving 50 million units of penicillin daily for a gram-negative septicemia. The penicillin was administered as the potassium salt. One million units contains 1.66 mEq. of potassium. This patient therefore received 83 mEq. of potassium daily by this means. Obviously, the sodium salt should be administered.

Even without exogenous supply, potassium from endogenous sources accumulates and poses one of the most important and dangerous complications to patients with acute renal failure. The increased plasma potassium results from the breakdown of cells or shifts of intracellular potassium. One liter of intracellular water contains 160 mEq. of potassium; 1 l. of red blood cells contains 100 mEq.[13] Therefore, necrotic tissue should be debrided. Infection should be treated.

The electrocardiogram is a more sensitive index of the cardiotoxic effects of hyperkalemia than is the serum potassium value. The toxic effects of potassium are accentuated by hypocalcemia, hyponatremia, acidosis and probably other unrecognized alterations. The electrocardiogram reflects the summation of these various parameters. The following progressive changes[7] may be observed:

1. Elevation and peaking of the T waves, first observed in the precordial leads, then in the limb leads.
2. Depressed ST segments.
3. Decreased amplitude of the R wave.
4. Prolongation of the QRS and the PR intervals.
5. Decreased amplitude and disappearance of the P wave.
6. Decreased amplitude of the T wave (as the QRS widens).
7. Mergence of the QRS and T waves into a sine wave.
8. Bradycardia, ventricular tachycardia, other arrhythmia or asystole.

These changes may develop with considerable rapidity as the oliguria continues. When the biochemical pattern is significantly disturbed, the electrocardiogram should be monitored every few hours.

Hyperkalemia may be combated in several ways. The synthesis of glucose to glycogen will remove potassium and phosphate from the plasma.[17] This process may be hastened by exogenous insulin (1 unit per 3 to 4 gm. of glucose). The insulin should be administered continuously to avoid hypoglycemia.

Calcium antagonizes the effects of potassium without changing the plasma level.[18] Calcium gluconate may be included in the infusion to form a 1 to 2 per cent solution when signs of the cardiotoxic effect of hyperkalemia are demonstrated by the electrocardiogram.

Sodium may reduce extracellular hyperkalemia by an incompletely elucidated physicochemical mechanism.[18,19] Hypertonic saline has been recommended as a temporary means of halting the cardiotoxic effect of potassium. Metabolic acidosis develops in these patients as uremia progresses. Metabolic acidosis is known to potentiate the toxic effect of potassium. Sodium chloride is an acidifying salt;[20] therefore, sodium lactate or bicarbonate would appear more effective. Bellet and Wasserman[19] reported dramatic changes in the electrocardiogram following the intravenous administration of molar sodium lactate. We have had similar experiences in this clinic (figure 1).

Cation exchange resins,* particularly the sodium cycle, have been extremely useful in our clinic. This preparation is available at present only for clinical investigation. The resin may be administered orally with small doses of chlorpromazine to prevent nausea and vomiting. The dose varies from 1 to 2 tablespoons (1 tablespoon equals about 9 gm.) every one to six hours, depending on the gravity of the situation, with just enough water to suspend the material. Considerable care must be exercised so that the patient does not become hyperhydrated with this therapy.

The resin also may be given by retention enema suspended in 10 per cent dextrose and

*Supplied by Dr. B. L. Martz, Clinical Research Division, Eli Lilly and Company Research Laboratories, Indianapolis.

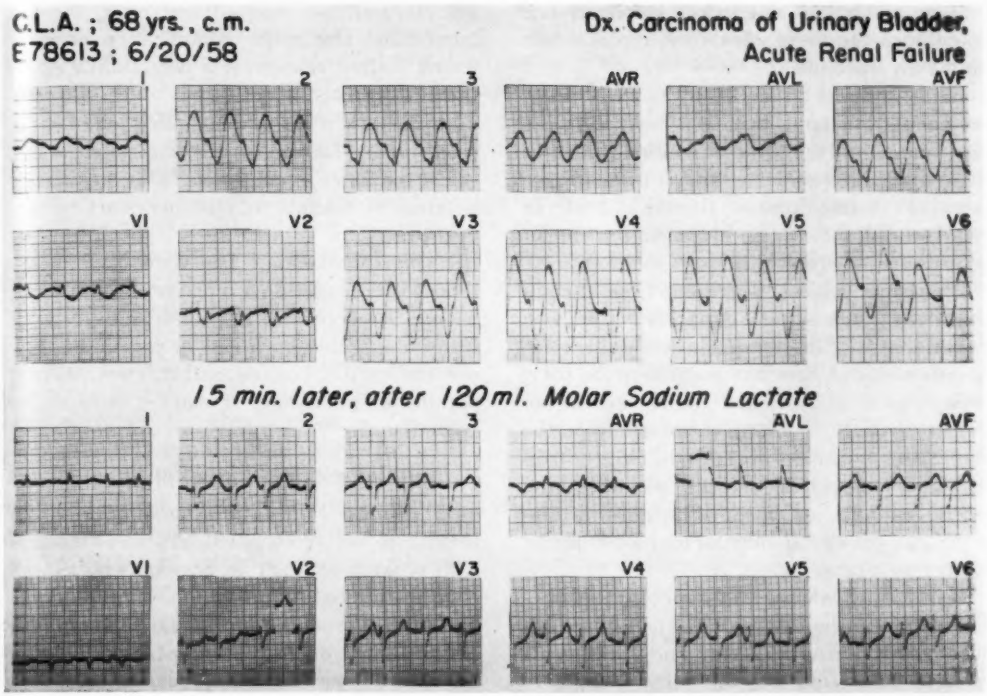

FIGURE 1. Electrocardiograms of a 68 year old Negro man in whom acute renal failure developed following transplantation of the ureters to an iliac pouch. The nonprotein nitrogen was 260 mg. per cent, sodium 126 mEq. per liter, potassium 6.7 mEq. per liter, chloride 81 mEq. per liter, and carbon dioxide 12 mEq. per liter.

Several minutes before the first electrocardiogram was obtained, the patient had a prolonged asystole and grand mal seizure. Cardiac action resumed concomitant with blows to the chest. The patient died the following day.

water. The sigmoid must be cleansed of the previously administered resin by a lavage of the bowel with 500 to 1000 ml. of 10 per cent dextrose solution. With this precaution, impaction has not been a problem nor has there been excessive uptake of water from the bowel when hypertonic solutions are used.

Androgenic steroids such as testosterone[21] and, more recently, NILEVAR® have been suggested as adjuncts in combating hyperkalemia. The efficiency of these hormones has never been established and they are not employed in this clinic.

The most effective means of combating hyperkalemia is artificial dialysis. Such an electrolyte alteration is one of the major indications for the use of the artificial kidney.

The relationship between digitalis and potassium has been clearly demonstrated.[22] The patient with acute renal failure *should not be digitalized unless absolutely necessary*, for, as the potassium level rises, the effect of digitalis decreases. When potassium is rapidly reduced by exchange resin or dialysis, the previously nontoxic amount of digitalis may become toxic and ventricular fibrillation and death may follow.

Hyponatremia—A moderate amount of hyponatremia usually develops in patients with acute renal failure. The lowered serum sodium may result from the movement of sodium into the intracellular space.[23] Usually, however, it is a reflection of dilution due to excess body water. The water of oxidation is salt-free. As indicated previously, a 70 kg. patient will produce about 500 ml. of such fluid daily. Profound hyponatremia frequently results from iatrogenic hyperhydration and is usually an

indication for fluid restriction. Hyponatremia potentiates the toxic effects of hyperkalemia on the myocardium.

Acidosis—The kidney in health excretes the net endogenous and exogenous hydrogen ion load poured into the blood.[24] This load amounts to 40 to 60 mEq. per day and is normally excreted as ammonium or titratable acid. In acute renal insufficiency, hydrogen ion cannot be excreted; therefore, acidosis develops.

Unless the acidosis is profound, no attempt should be made toward correction. It is well known that the carbon dioxide-combining power does not always reflect accurately the pH.

Acidosis is of particular significance in potentiating the toxic effects of potassium on the myocardium. Should progressive electrocardiographic changes be present, molar sodium lactate may be indicated. If acidosis is corrected, supplemental calcium may be required to prevent tetany.

Hyperphosphatemia and hypersulfatemia—These nonvolatile ions, sulfate and phosphate, accumulate during oliguria. They have been referred to as acid ions and were thought to be the cause of uremic acidosis. It has been pointed out, however, that sulfate and dibasic phosphate (the form of most of the retained phosphorus) are actually weak bases or proton acceptors rather than acids. One may elevate serum phosphate or sulfate concentrations in normal subjects by infusing buffered solutions of sodium sulfate or sodium phosphate without effecting any change in the acid-base balance of the blood.[23] The effect of these ions in patients with acute renal failure has not been completely elucidated.

The phosphate absorption from the gastrointestinal tract may be reduced by AMPHOJEL®.[8] As the phosphate level rises, calcium decreases. The phosphate level is not reduced by administration of calcium.

Meroney and Herndon[18] reported that the phosphate level is a useful index of the presence of necrosis. A plasma phosphorus of 10 mg. per cent with a nonprotein nitrogen less than 150 mg. per cent suggests severe tissue destruction. We have observed a similar correlation in two cases in this clinic.

Hypocalcemia—As the phosphate level in the extracellular compartment rises, the calcium falls. The major complication of a reduced ionized calcium is a potentialization of the toxic effects of potassium on the myocardium. Tetany is rarely a complication of acute renal failure because of the associated acidosis. If the latter is corrected, however, administration of calcium may be necessary to prevent tetany.

Hypermagnesemia—The significance of alterations of magnesium remains obscure. Magnesium is second only to potassium in terms of intracellular concentration. In acute renal failure the serum concentration rises, usually parallel to potassium. It can be reduced by hemodialysis.[25]

Hematologic Abnormalities

1. *Anemia*—The association of anemia with uremia is well recognized. Anemia develops with striking rapidity in persons who experience acute renal failure from any cause. Swan and Merrill[7] stated that a rapidly progressive anemia is one of the most constant features of the clinical course of acute renal failure. However, the presence of a normocytic, normochromic anemia during the first several days of anuria or oliguria suggests underlying chronic renal disease.

The anemia is usually of only moderate severity (hematocrit 20 to 25 per cent). Having reached this level, the progression slows or stops despite persistence of oliguria.

The anemia is well tolerated by most patients. Transfusion is rarely indicated. Transfused cells have a shortened survival time,[26] and the destruction of red cells is accompanied by liberation of potassium. The possibility of overloading the circulation by a transfusion must be considered prior to the administration of blood. If oxygen transport is inadequate, fresh packed cells should be infused slowly. The volume of the transfusion must be considered as part of the fluid for that day.

The mechanism of the anemia remains obscure.[27] There is evidence to support the theory that it is due to both a hemolytic and an aregenerative component.[28] It also has been suggested that damaged kidneys fail to manufacture or activate an erythropoietic factor.[29]

2. *Bleeding tendency*—Rath, Mailliard and Schreiner[30] reviewed the problem of bleeding accompanying uremia. They reported that 18 of 21 patients with acute renal insufficiency had clinical bleeding. Bleeding was a contributory cause of death in five patients. The exact mechanism remains obscure; however, a defect in platelets appears to be the most constant abnormality.

It was suggested that the transfusion of fresh platelets may be of value. Meroney and Herndon[18] reported that the bleeding tendency was not altered by hemodialysis. However, limited experience in this clinic suggests that this procedure may in some cases ameliorate the bleeding tendency. Bleeding per se does not pose an absolute contraindication to hemodialysis. Heparinization necessary for dialysis does not increase bleeding. The possibility that a bleeding tendency will develop as the uremia progresses makes hemodialysis desirable earlier in the course of the illness.

Infection

Infection increases catabolism and must be prevented or controlled. Weinstein[31,32] reported that chemoprophylaxis may be of little value in preventing bacterial complications in bulbar poliomyelitis and measles. The superinfection which often may develop is caused by resistant organisms.

Antibiotics should be used to treat only specific infections. Agents with nephrotoxic properties, such as bacitracin and neomycin, are contraindicated. Agents requiring good kidney function for excretion should be used with caution. For example, approximately 70 per cent of parenterally administered streptomycin is excreted by the kidney within 24 hours by patients with good function.[33] When kidney function is severely impaired, the plasma level may remain elevated for several days. If medication is continued, serious toxic effects appear. One to two grams of streptomycin every other day is probably safe if not administered for more than six to eight doses.

Caution should be exercised in changing surgical dressings. Cutdowns should be avoided if possible. Respiratory isolation is indicated. If the tracheobronchial tree requires aspiration, aseptic technics should be used.

Urinary catheters are strongly contraindicated if the patient can void and is cooperative.[34] Kass[35] reported that bacilluria developed within four days in 95 per cent of the patients who had indwelling catheters; most cases developed within the first 24 hours. The bacilluria could not be prevented by the prophylactic use of antibiotics.[36] At times, however, the catheter is indispensable. It should never be employed simply for the convenience of the attending physicians and nurses. When used, the catheter and urethral orifice should be protected from unnecessary contamination. Kass and Schneiderman[37] suggested that the route of entry of bacteria to the bladder is around the catheter in the exudate that forms in the urethra rather than through the lumen of the catheter.

Because of increased catabolism, fever should be reduced by sponging and by use of salicylates.

Cardiovascular Complications

The major concern of the clinician in managing patients with acute renal failure is to prevent water intoxication, congestive heart-failure and fatal arrhythmias or asystole.

Water intoxication and congestive heart-failure usually result from the administration of excessive fluid to a patient with a "closed system." They are therefore iatrogenic complications. In the past, such complications have been the major cause for the mortality[7] of 80 to 90 per cent[4] of patients with acute renal failure. Muirhead, Vanatta and Grollman[38] in 1949 reviewed the management of such patients and reported that frequently 5 to 7 l. of fluid per day was administered despite a negligible output.

Meticulous attention to fluid intake can prevent congestive heart-failure in most cases. Careful daily auscultation of the lungs and heart is imperative. Accentuation of the pulmonic second sound or the appearance of a protodiastolic or presystolic gallop indicates impending failure. Distention of the neck veins and fingerprint and pitting edema are indications of hyperhydration. Determination of the venous pressure is frequently helpful.

Hyperhydration with or without associated congestive heart-failure can best be treated by fluid restriction. Diuretics are useless and may be nephrotoxic. Digitalis is usually ineffective, for it cannot initiate a diuresis. Should it be indicated because of supraventricular tachycardia, short-acting preparations in about two-thirds the average digitalizing and maintenance dosages are indicated.

Fibrinous pericarditis with an associated rub is not uncommon. Wacker and Merrill[39] reported an incidence of 18 per cent. The sign does not have the same prognostic significance as it does in chronic renal failure.

Other Complications

Patients with acute renal failure frequently have a variety of troublesome symptoms such as anorexia, nausea, vomiting, diarrhea and abdominal distention. Such symptoms should be treated with caution. No medication should be administered without evaluation of its route of excretion and potassium content.

Somnolence, stupor, muscular weakness, restlessness and apprehension are not uncommon symptoms. They usually reflect the degree of uremia. Muscular wasting and asthenia may be profound, especially in older patients, and recovery of strength after diuresis may be extremely slow.

Maintaining a patient without oral intake for several weeks may occasionally result in acute parotitis or cholecystitis due to inspissation of the ducts of these organs. Such rare complications occur most frequently in elderly persons. Parotitis may be prevented by having the patient suck hard candy or a lemon slice.

It must be remembered that not all symptoms are due to uremia. Infection must be combated. Pneumonia is one of the major complications leading to death. Anoxia and hypotension must be avoided. The airway must be maintained.

Artificial Dialysis

If properly managed most patients without trauma, extensive surgery or infection in whom acute renal failure develops will survive long enough for the renal lesion to heal and for adequate renal function to return. However, with complications which increase catabolism, the patient may die before the nephrons recover adequate function. Artificial means of removing toxic products must be used to gain time to permit adequate healing to take place.

Most clinics prefer to use the artificial kidney instead of peritoneal lavage or other more cumbersome and less effective means. The usefulness of hemodialysis has been adequately demonstrated.[40] A discussion of the advantages and disadvantages of the various artificial kidneys available is beyond the scope of this paper.

The indications for dialysis vary from patient to patient. In our clinic we consider progressive hyperkalemia, profound acidosis, bleeding tendency and increasing stupor as the major indications. Complications which develop as uremia increases can be avoided by hemodialysis. The ultrafiltration characteristics of the Kolff coil-type instrument permit the removal of significant quantities of fluid. Therefore, hyperhydration becomes a relative indication.

Diuretic Phase

The diuretic phase begins when the daily urinary volume exceeds 400 ml. The onset of diuresis does not indicate that meticulous management of the patient is no longer necessary. Swan and Merrill[7] reported that 25 per cent of the deaths in their series occurred after the onset of diuresis. They suggested that enormous urinary outputs reported during this phase of the disease are the result of hyperhydration during the oliguric phase. It is now generally agreed that the problems of management of the diuretic phase are determined by the state of hydration when the diuresis begins.

These patients are unable to concentrate urine. Finkenstaedt and Merrill[41] showed that they have a delayed response to water loading. The clearance of insulin, thiosulfate, mannitol, creatinine, para-aminohippurate and iodopyracet (DIODRAST®) are decreased.

Management of the diuretic phase requires careful weighing and determination of output and intake. The volume of the urine output need not be replaced if the patient is hyper-

hydrated. Careful clinical evaluation of the state of hydration of the patient is imperative. Administration of sodium, chloride and potassium becomes necessary once the diuresis begins; however, the amount must be determined according to the individual patient. Determinations of urinary sodium, potassium and chloride are helpful. Suddenly changing to large, orally administered volumes frequently results in nausea and vomiting. Parenteral alimentation should be continued until adequate oral intake is possible.

Prognosis

The ultimate return of function depends on the extent and type of initial injury to the nephrons or that subsequently sustained because of anoxia or injudicious administration of nephrotoxic medications. The reparative process of the nephrotoxic lesions is relatively simple. If the basement membrane is intact, a new inner tubing of epithelial cells may easily form. Areas of tubulorhexis, with disruption of the basement membrane, are more complex. Oliver[6] demonstrated that a patch of two tissues, epithelial and mesenchymal, must be organized to re-form the tubule wall. Undoubtedly, this cannot always occur. Many nephrons containing extensive tubulorhexic disruptions never again become functioning units. These lesions are distributed in a random fashion. Unless very numerous, the loss of such nephron units cannot be detected by currently available function studies. Permanent damage may remain, but hypertrophy and hyperplasia may compensate to some extent for the function that was lost. If the damage was extensive, healing may be associated with a significant deficit of functioning nephron units. However, progressive pathologic changes apparently do not develop after clinical healing from the initial insult has occurred.[41]

The continuity of the tubules is probably established promptly, but a considerable period is required for maturation of the regenerated cells so that they function normally. Renal function may continue to improve gradually and approach normal proportions within 6 to 12 months.

Lowe[42] reported a long-term follow-up of 14 cases of acute renal failure. Clinical recovery was satisfactory in the entire group. However, clearance values remained below the lower limits of normal for as long as three years. Finkenstaedt and Merrill[41] reported a follow-up of 16 patients who were selected for study because of absence of any cardiovascular or renal disease before the acute episode. These observations are in general agreement with those of Lowe.

Summary

Acute renal failure is a syndrome due to a variety of etiologic mechanisms. The ultimate recovery of the patient depends on the nature of the initial insult to the kidneys, the physiologic state of the kidneys prior to the insult, the judicious management by the physician, and other ill-defined events. In general, if there is a question as to whether a medication or other therapy is indicated, it is better to withhold it. In few conditions is the string joining life and death more tightly drawn, acts of omission better tolerated, and acts of commission more serious.

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Modern Treatment of Common Intestinal Parasitic Diseases

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Approximately 40 million Americans harbor parasites at the present time. Involvement may be so slight that no symptoms are clinically evident, or the parasite may produce symptoms typical of severe intestinal disease.

The author discusses therapeutic agents and regimens he has found to be effective in treating amebiasis, giardiasis, intestinal trichomoniasis, ancylostomiasis, ascariasis, enterobiasis, strongyloidiasis, trichuriasis and tapeworm infection.

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In some parts of the United States diseases caused by parasites are considered relatively common, whereas in other areas clinicians believe that their communities are relatively free of this type of infection. These geographical variations reflect more the physicians' interests and training in problems involving parasites than they do the true prevalence of infection. If one accepts conservative estimates of the incidence of the more common parasitic conditions, including enterobiasis, vaginal trichomoniasis, trichinosis and amebiasis, approximately 40 million United States citizens harbor parasites at the present time.

With increased international travel, with the influx of almost one million Puerto Ricans into the United States mainland, and with the increased interest of American physicians in global medicine, it may be assumed that diagnostic alertness toward parasitic infections is increasing.

The purpose of this paper is to present a summary of the most recently developed drugs and technics which are available for eliminating or controlling the more common intestinal parasites. Progress in treating parasitic infections has not been as dramatic as have

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been the accomplishments in antibacterial therapy. Nevertheless, certain significant advances within the past few years make it desirable to review the current therapeutic programs.

Amebiasis

Estimates of the prevalence of amebiasis in the United States vary from less than 2 per cent to over 20 per cent. More important than the difference in the reported prevalence of amebiasis is the widely recognized disparity between the relatively large number of persons who harbor *Endamoeba histolytica* in their stools and the small number who have symptoms of disease. Some authorities hold to the view, widely accepted in Great Britain, that there are two subspecies or races of *E. histolytica:* (1) a small, relatively common race, which does not produce intestinal disease, and (2) a larger, less common variety, which is responsible for the clinical syndrome. Recent work has indicated that the two subspecies or races are not as distinct as has been reported; one can be changed into the other under experimental conditions. I believe that the presence of *E. histolytica* in the stool indicates intestinal infection; however, in a large number of persons the degree of intestinal involvement is so slight that either no symptoms reach the clinical horizon or they are so minor as to be generally considered insignificant. If this view of the pathogenicity of *E. histolytica* is accepted, then all patients with this infection should be treated, especially since an intestinal infection may lead to the occurrence of metastatic lesions in the liver.

The wide range of therapeutic agents available for the treatment of amebiasis includes emetine hydrochloride, administered intramuscularly; emetine bismuth iodide, administered orally; antibiotics such as the tetracyclines, fumagillin, bacitracin and others; the halogenated quinolines, DIODOQUIN®, VIOFORM® and chiniofon (YATREN®); arsenicals, the most popular being carbarsone, MILIBIS® and BALARSEN®; quinacrine hydrochloride (ATABRINE® dihydrochloride), and chloroquine phosphate (ARALEN® diphosphate).

The following regimen represents a full and satisfactory course of therapy for intestinal amebiasis. Emetine hydrochloride, in a dosage of 60 mg. given intramuscularly once daily for five consecutive days, is administered concurrently with a dosage of 250 mg. carbarsone given four times a day for 10 days. At the end of this period, either tetracycline (250 mg. four times a day for 7 to 10 days) or Diodoquin (0.6 gm. four times a day for 14 days) may be given. If there is any evidence of metastatic amebiasis, i.e., hepatic amebiasis, 0.5 gm. chloroquine phosphate should be given twice a day for two days and then once a day for 14 to 16 days. When *E. histolytica* is found in the stool of an asymptomatic patient during a routine checkup, administration of emetine hydrochloride is unnecessary, and only carbarsone and either tetracycline or Diodoquin need to be given.

Although the present discussion is concerned mainly with the treatment of intestinal parasitism, the treatment of amebic abscess of the liver should be mentioned briefly. When an abscess is present, it is advisable to administer both emetine hydrochloride and chloroquine phosphate; 60 mg. emetine hydrochloride is given intramuscularly each day for 10 days and is followed by chloroquine phosphate administered for two to three weeks according to the dosage schedule previously outlined. This course should be repeated after three months.

Both patients and physicians frequently express fear that intestinal amebiasis is virtually incurable. The program outlined here or a similar one will produce cures in over 90 per cent of patients. Most patients with "incurable" or "intractable" amebiasis are the victims of a mistaken diagnosis. Occasionally, it is exceedingly difficult to distinguish between trophozoites and macrophages, and it is not as easy to identify cysts of *E. histolytica* as might appear from the discussions in textbooks.

Giardiasis

Infection with *Giardia lamblia* is much more common than is generally recognized and causes severe and disturbing diarrhea. In addition, the parasite, which lives in the duo-

denum and jejunum, often involves the biliary tract. Thus, it may produce either upper intestinal symptoms including dyspepsia or syndromes simulating disease of the gallbladder, gastritis, peptic ulcer or psychosomatic conditions. Treatment consists of 100 mg. quinacrine hydrochloride (Atabrine dihydrochloride) given three times a day for 7 to 10 days. After 7 to 10 days of treatment, a slight yellowish staining of the skin will begin to develop in some fair-skinned patients. They should be warned about this in advance in order to forestall fears about hepatitis. A single course of therapy will produce a cure in about 80 to 85 per cent of patients. A second course may be administered after an interval of 10 days. If two courses of therapy with quinacrine hydrochloride fail, chloroquine phosphate may be tried, using a dosage of 1 gm. daily for two days followed by 0.5 gm. daily for another seven days. The arsenicals and antibiotics do not eliminate this parasite.

Intestinal Trichomoniasis

This condition is caused by *Trichomonas hominis*, a parasite which should not be confused with the much more common *T. vaginalis*. Occasionally, *T. hominis* may cause severe diarrhea. It may be eliminated by giving either an arsenical such as carbarsone in a dosage of 250 mg. four times a day for 7 to 10 days or tetracycline in a dosage of 1 gm. daily for the same period.

Ancylostomiasis

Hookworm is encountered only rarely in persons living in the continental United States. However, it is still widespread in the tropics and is seen often in visitors from other countries. Although the roster of antihookworm agents is almost as long as that for intestinal amebiasis, only tetrachloroethylene can be recommended at present.

The patient receives a simple fat-free supper. The next morning, in place of breakfast, he is given four 1 ml. capsules of tetrachloroethylene. After an interval of three hours, a saline cathartic, such as 30 gm. sodium sulfate, is administered. Recent reports have suggested that the saline cathartic is unnecessary, but its use should be continued until further evaluation has been completed. This treatment will cure most cases of infection by *Necator americanus*. However, if the more persistent *Ancylostoma duodenale* is the infecting parasite, it may be necessary to repeat this regimen either once or at weekly intervals on several occasions. In repeating the course of therapy, it is preferable to give tetrachloroethylene again rather than to shift to one of the more toxic preparations.

In the near future, a new drug, one of a group of bephenium compounds, will be available and will be worthy of trial. Bephenium hydroxynaphthoate (trade name in the United Kingdom, ALCOPARA®), bephenium iodide and bephenium emboate have considerable uncinariacidal activity. The toxicity of these preparations is slight, and their administration is simple. However, dosage schedules and efficiency values have not yet been established for these agents.

Ascariasis

Ascaris lumbricoides is one of the most dangerous of the parasites infecting humans. Compounds such as santonin, chenopodium oil and diethylcarbamazine citrate (HETRAZAN®) which were formerly used for treatment are no longer recommended.

Piperazine, as the citrate, diphenylacetate, phosphate, etc., is currently the drug of choice. The recommended daily dosage for piperazine citrate is as follows: for patients weighing up to 30 lb., 1 gm.; 30 to 50 lb., 2 gm.; 50 to 100 lb., 3 gm.; over 100 lb., 3.5 to 4 gm. Single doses in wafer or syrup form may be given for two consecutive days and may be repeated after one week. Accessory purgation is unnecessary. Side effects are minimal; only an occasional patient experiences nausea, vomiting, urticaria, general muscle weakness or blurred vision. These symptoms quickly disappear when the drug is stopped.

Hexylresorcinol, although ascaricidal, is moderately toxic. It is taken in capsule form in the morning on an empty stomach, the dosage schedule being 1 gm. for adults, 0.8 gm. for children 6 to 10 years of age, and 0.6 gm.

for children under six years. A saline purge given two hours later facilitates removal of dead and dying worms. To prevent gastric colic and ensure greater efficacy of the drug, food should be withheld for four to five hours after administration of the drug.

Three new preparations being studied as to efficiency and dosage in the treatment of ascariasis are dithiazinine iodide (Delvex), bephenium hydroxynaphthoate (Alcopara), and pyrvinium pamoate (POVAN® suspension).

Enterobiasis

Enterobius vermicularis, commonly called pinworm or threadworm, is prevalent in temperate climates; between 20 and 25 million children are infected in the United States. The protracted course of the disease and the difficulty in effecting a cure are due to the ease of reinfection. Rigid enforcement of hygienic measures accompanied by simultaneous treatment of other members of the household, who serve as a reservoir for reinfection, is necessary for successful treatment.

Of the medications available for treatment, the unsubstituted piperazine salts, available in wafer or syrup form, have an approximate rate of cure of 80 per cent or greater. Piperazine is given once daily for seven consecutive days according to the following dosage schedule: for children weighing up to 15 lb., 250 mg.; 15 to 30 lb., 500 mg.; 30 to 60 lb., 1 gm.; over 60 lb., 2 gm. Treatment may be repeated after one week or at regular intervals, e.g., every three months, to keep the worm population low in those patients who become reinfected.

Pyrvinium pamoate (Povan suspension, formerly Poquil and Vanquin) may replace piperazine as the drug of choice for treating enterobiasis. Chemically, it is the bis-6-dimethylamino-2-[2-(2,5-dimethyl-1-phenyl-3-pyrrolyl) vinyl]-1-methylquinolinium salt of 4,4′-methylenebis (3-hydroxy-2-naphthoic acid), a complex cyanine dye. It is available as a coated tablet containing 100 mg. of the anhydrous pyrvinium base and also as a red, strawberry-flavored suspension containing the equivalent of 10 mg. of base per milliliter. Since the drug is not absorbed from the intestinal tract, it colors the stool bright red; if spilled, the suspension will stain clothing and other materials.

A single dose of pyrvinium pamoate will cure enterobiasis in over 90 per cent of the cases. The recommended dose is 5 mg. of the anhydrous pyrvinium base per kilogram of body weight. One teaspoonful (5 cc.) of the suspension per 22 lb. (10 kg.) of body weight or one 100 mg. tablet per 40 lb. of body weight may be given. Since overdosage is not dangerous, it is safe to add a dose unit for any proportion of 20 or 40 lb. For example, a child weighing 50 lb. may be given three teaspoonfuls (15 cc.) of the suspension, and an adult weighing 140 lb. may be given four 100 mg. tablets. Toxic symptoms, including nausea, vomiting and diarrhea, rarely occur.

In addition to treatment with piperazine or pyrvinium pamoate, the following adjuvant measures are recommended:

1. A daily morning shower to remove eggs deposited in the perianal region during the night.
2. Regular application of an antipruritic ointment over the perianal area at bedtime. An ointment of mercury in petrolatum or PERAZIL® hydrochloride cream (1 per cent chlorcyclizine hydrochloride) is excellent.
3. Use at night of closely fitting shorts under one-piece pajamas closed securely by ties or safety pins.
4. Regular trimming of the child's nails and regular scrubbing of his fingers with a brush following use of the toilet.
5. Daily disinfection of the toilet seat.

The use of antibiotics, gentian violet medicinal (methylrosaniline chloride), tetrachloroethylene, phenothiazine, Egressin, high enemas, gamma benzene hexachloride, infusions of quassia chips, and antihistamines is not recommended.

A cure of enterobiasis is considered to have been achieved when cellophane swabs placed on the perianal region show no oxyurid ova for seven consecutive days. The swabs are taken each morning prior to bath or bowel movement, starting one week after completion of therapy. Two or three negative swabs are adequate in clinical practice.

Strongyloidiasis

Strongyloides stercoralis, common in warm climates, occurs also in temperate and even cold regions. Intestinal symptoms include abdominal discomfort, dyspepsia, diarrhea, tenderness of the liver, and eosinophilia.

The drug of choice for treating strongyloidiasis is dithiazinine iodide, available commercially in 50, 100 and 200 mg. tablets. The dye is blue and only slightly soluble in water; since it usually is not absorbed from the intestinal tract, it often stains the stool blue. The exact rate of cure is not yet established, but may be about 50 per cent. Dithiazinine iodide is also effective against infection with *Trichuris, Enterobius* and *Ascaris*.

Dithiazinine iodide is administered three times daily for 10 to 14 days, the total daily dosage being as follows: for children weighing 20 to 30 lb., 200 mg.; 30 to 40 lb., 300 mg.; 40 to 50 lb., 400 mg.; 50 to 60 lb., 500 mg.; adults and children over 60 lb., 600 mg.

In my experience, acceptance of dithiazinine iodide by the patient has been poor, despite the fact that careful clinical studies have shown no evidence of renal, hepatic or hematopoietic damage following its administration in therapeutic doses. However, intense nausea, vomiting and abdominal cramps with diarrhea have occurred on the first day of treatment, making continuation difficult. In these cases, the following modifications of the originally recommended program have been effective: (1) treatment for twice as long using one-half the recommended dose and (2) administration of an antiemetic and tranquilizer, such as prochlorperazine dimaleate (COMPAZINE®), the day before treatment is started and for the first four days of therapy.

Gentian violet medicinal has been reported to be effective in treating strongyloidiasis and may be administered orally in the form of enteric-coated tablets. The dosage for adults is 65 mg. given three times a day with meals for 16 days. In children, it is advisable to administer daily for 16 days 10 mg. of the drug for each year of the child's age. Nausea, vomiting and colicky pain in the abdomen may accompany administration of this drug. If patients show a poor response to oral therapy, 25 ml. of a 1 per cent solution of the drug may be given by transduodenal intubation in place of tablets. Intravenous administration of gentian violet is dangerous.

Diethylcarbamazine citrate (Hetrazan), given orally in dosages of 2 mg. per kilogram of body weight three times daily for 20 days, is rarely successful in treating strongyloidiasis.

Trichuriasis

A mild infection with *T. trichiura* (whipworm) may be regarded as innocuous and does not call for energetic treatment.

Dithiazinine iodide is effective against trichuriasis, with the possible rate of cure being almost 75 per cent. This rate is dependent, however, on reducing to a minimum the drug's toxic manifestations, especially those occurring on the first or second day of its use. The dosage schedule is identical with that used in the treatment of strongyloidiasis, but therapy need be maintained for only 5 to 10 days. The advisability of concurrent use of Compazine and other preparations has been discussed.

A high-retention enema with hexylresorcinol may be used when there is a heavy infection by *Trichuris*. Following a preliminary enema to clear the large intestine of fecal accumulation, the perianal area and buttocks should be coated with petrolatum to prevent superficial burns with hexylresorcinol. The retention enema is then given and consists of 1 gm. hexylresorcinol in about 500 ml. water at body temperature to which 30 gm. of fine kaolin may be added to minimize colonic cramps. The procedure may be repeated in one week.

Tapeworm Infection

Four major types of cestodes inhabit the intestinal tract of man: *Taenia saginata* (beef tapeworm), *T. solium* (pork tapeworm), *Diphyllobothrium latum* (fish tapeworm), and *Hymenolepis nana* (dwarf tapeworm). These worms cause vague gastrointestinal and nervous symptoms and may initiate bizarre systemic disturbances due to mechanical irritation. They also produce toxic products and are able to deprive the host of nutritional requirements. *T. solium* is dangerous, since its

larvae may migrate to all organs of the body and form a stage called *Cysticercus cellulosae* which is not amenable to drug therapy.

Because of its high degree of efficacy and relatively low toxicity, quinacrine hydrochloride is the drug of choice. Since the drug acts as a gastric irritant and may cause nausea and vomiting when taken orally, it is best administered by transduodenal intubation. This procedure ensures a greater concentration of the drug at the required site and reduces the risk of vomiting. In infection with *T. solium*, reverse peristalsis, initiated by gastric irritation, may facilitate the movement of eggs from the jejunum into the duodenum. Since this increases the danger of cysticercosis, medicaments should always be given by intubation in treating this infection.

Careful preparation of the patient is necessary for successful treatment. The patient is given a light lunch and a liquid fat-free supper on the day before treatment. Early the next morning, on an empty stomach, the patient takes orally a sedative such as 60 mg. phenobarbital. A duodenal tube is then inserted. One hour later, 1 gm. quinacrine hydrochloride suspended in 20 ml. water is introduced through the duodenal tube and is washed down with a small amount of water to prevent loss of the drug in the syringe and tube. If the drug is administered orally, 2 tablets (0.2 gm.) are given at 10 minute intervals for a total of 10 tablets (1 gm.); a little sodium bicarbonate is added to each dose to counteract the emetic impulse which often accompanies oral medication. A saline purgative such as 30 gm. sodium sulfate is given two to four hours after the drug is administered. If satisfactory purgation is not achieved, a soapsuds enema should be administered. A normal diet may be resumed following this treatment.

All stool specimens should be examined carefully for the scolex of the worm for 72 hours following therapy. Usually, the intact worm with the scolex attached is passed within 12 hours. Inability to find the scolex does not necessarily indicate that the treatment has failed, since the scolex may have become lodged temporarily in the large intestine or may have been digested or lost. If the scolex is not found, the absence of segments and eggs in the stool for a six month period after treatment may be accepted as the criterion of cure. The rate of cure is over 90 per cent with this technic. Occasionally, more than one worm will be present.

Rosen and Kiefer have recently published the following modification of a method developed by DeRivas in 1932:

> Before the treatment is begun, the following articles should be ready at the bedside: (1) A Rehfuss tube, (2) a 50 cc. syringe, (3) a bottle of glycerin, (4) a bottle of saturated magnesium sulfate solution, (5) a thermometer (preferably centigrade), and (6) 500 cc. of sterile saline solution.
>
> The procedure for treatment is as follows. (1) Pass a Rehfuss tube into the stomach. (2) Turn the patient on his right side and allow the tube to pass into the duodenum. (3) Check the tube by fluoroscope to be certain that the tip is well down in the second or third portion of the duodenum, beyond the ampulla of Vater. (4) When certain the tube is in position, introduce 1½ oz. of magnesium sulfate solution through the tube. (5) Then introduce immediately 1½ oz. of glycerin. (6) Then introduce immediately 2 oz. of a mixture of equal parts of magnesium sulfate and glycerin. (7) Then introduce immediately 500 cc. of the sterile saline solution, which has been warmed to a temperature of 54-60° C. or 130-140° F. A bucket and a bedpan should be ready in the patient's room. The bucket should contain warm water or saline solution so that if the worm is obtained, it can be preserved and identified.

Of the 40 patients treated in this manner, 36 were considered cured and the scolex was present in 31. No evidence of infection was found in five patients in the follow-up periods that ranged from one to five years.

Aspidium oleoresin is also effective against a tapeworm infection. A mixture of 6 gm. of freshly prepared aspidium oleoresin, 30 ml. acacia, and 30 ml. of a concentrated solution of sodium sulfate is administered through a duodenal tube. After this treatment, no purgative is necessary but its use may be desirable in order to expel the head of the worm. The drug also may be administered orally, a dose

of 1.2 ml. being given every 30 minutes until the patient has received 3.6 ml. This is followed in two hours by a saline purge. However, the difficulty of obtaining freshly prepared aspidium oleoresin and the drug's high toxicity are arguments against its use.

The treatment of a tapeworm infection in children remains a problem. Since the therapeutic dose and the toxic dose approximate each other, the reduction of the dose to levels tolerated by children prevents successful treatment. Some promising results have been achieved with iodoalphionic acid (PRIODAX®), a drug used for visualization of the gallbladder. The recommended dose, and one that is well tolerated, is 3 gm. for children weighing 40 lb. or less, 4 to 5 gm. for children weighing 41 to 99 lb., and 6 gm. for children weighing 100 lb. and over.

Since the measures outlined have been relatively ineffective against the dwarf tapeworm, *H. nana*, some practitioners recently have begun to use chloroquine phosphate. However, uniformly successful results have not been obtained.

Comment

For purpose of practicality, the foregoing regimens have been presented in a didactic, almost arbitrary fashion. With reports on the efficacy of so many drugs coming from so many different countries and different research centers, it is difficult to suggest specific courses of therapy without being dogmatic. The recommendations which I have made are based on my personal experience, with full recognition that satisfactory alternatives also may be available.

1960

INTERSTATE POSTGRADUATE MEDICAL ASSEMBLY

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LESTER ADELSON, M.D.

Assistant Professor of Legal Medicine, Western Reserve University School of Medicine, Cleveland

Major hazards faced by the medical witness in his infrequent court appearances stem from his lack of familiarity with the judicial process, his morbid fear of cross examination, and the absence of a sound philosophy to direct him in his testimony. This presentation will attempt to clarify the role of the physician who testifies in the capacity of expert witness. An impartial approach to the evidence and the development of a healthy attitude toward the judicial process will be stressed. This should lead to better medical testimony, improvement in the administration of justice, and more realistic verdicts.

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Cystosarcoma Phyllodes

JOHN CARPATHIOS* AND ALAN RAFTERY†

Mercy Hospital and Timken Mercy Hospital, Canton, Ohio

Cystosarcoma phyllodes is usually a nonmalignant tumor which the authors believe occurs more often than the literature reports on it indicate.

If the tumor is relatively limited in extent and well encapsulated, wide excision is the accepted method of treatment.

Simple mastectomy should be performed if the tumor recurs locally after its excision.

If there is evidence of malignant transformation, radical mastectomy should be done.

THIS rather rare, usually nonmalignant tumor of the breast was first described by Johannes Müller[1] in 1838. About 320 cases of this tumor have been reported in the literature, but we believe that it occurs much more frequently than such reports would indicate. The tumor is known by various names such as giant adenofibrosarcoma, intracanalicular myxoma, intracanalicular adenofibroma and fibromyxoma. In this paper, we shall use the term cystosarcoma phyllodes since we believe it is used most frequently by pathologists and surgeons.

Clinical Picture

In many cases, cystosarcoma phyllodes seems to originate from a pre-existing fibrosarcoma which may have been present for many years. It has been noticed that menstruation and pregnancy act as stimuli for the start of the tremendous increase in the size of the tumor in some cases. In other cases, however, the tumor grows rapidly after it becomes evident.[2] It usually occurs in women who are between 25 and 50 years old. It usually involves only one breast, but there are reports of cases in which both breasts were involved.

Rapid and massive enlargement of the tumor is one of the most characteristic clinical features. The tumor is usually freely movable, is not attached to the skin, and does not cause retraction of the nipple. In some cases, the contour of the breast may become distorted owing to the rapid growth of the tumor. The tenseness of the skin may increase until rupture occurs because of pressure necrosis. Ul-

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ceration, bleeding or infection then may occur. In cases in which ulceration occurs, a funguslike lesion may penetrate the skin and simulate an advanced malignant lesion.[3]

Pathology

The tumor usually is well encapsulated, freely movable, and is not fixed to the skin or underlying tissues. It is often lobulated and consists of a strange combination of firm tissue, soft gelatinous tissue, and cysts. Histologically, it has most of the features of a sarcoma. Because of the marked variation in the stromal pattern within a single tumor, many sections should be examined microscopically. The wide variety of the gross and microscopic appearance of this tumor obviously accounts for the many names used to designate it.

Although this tumor usually is benign, the literature contains reports of several cases in which the tumor has recurred locally after its removal. In rare cases, it may behave like a malignant tumor and involve the lymph nodes and metastasize to the lungs and bones.[4] The literature contains reports of about 35 cases in which the tumor has acted in this manner. Reich and Solomon[5] reported a case in which a malignant tumor of this type occurred in each breast. Many authors agree that the tumor remains localized for some time in the rare cases in which malignant transformation occurs, but metastasis eventually occurs to the regional lymph nodes and to distant sites.

Treatment

If the tumor is relatively limited in extent and is well encapsulated, wide excision of the tumor is the accepted method of treatment. If the tumor should recur locally after its excision, simple mastectomy should be performed. This also is the operation of choice in cases in which the tumor is bulky, nodular and expansile, but dissection of the axillary lymph nodes usually is not necessary in these cases. If the tumor shows evidence of malignant transformation, that is, if it involves the overlying skin or underlying muscles or metastasizes to distant sites, radical mastectomy should be performed.

In discussing the treatment of this confusing tumor, we want to emphasize the danger of hastily and erroneously diagnosing a huge cystosarcoma phyllodes as an inoperable malignant tumor. We almost made this diagnostic error in one of our cases. On the other hand, one always must be alert not to overlook the rare occurrence of a malignant variant of this type of tumor. In cases in which this malignant variant is present, radical operation undoubtedly will increase the life expectancy of the patients.

Case Reports

Case 1—A white married woman, aged 49 years, was admitted to the hospital because of a lump which had been present in the lower outer quadrant of the left breast for six months. She had been asymptomatic until three weeks before her admission to the hospital. At that time, she had noticed a rapid growth of the lump and increasing tenderness and redness over the involved portion of the breast.

The left breast was considerably enlarged, and the lower portion was red and tender to palpation. The nipple was not retracted, and the lump was not fixed to the skin. There was no evidence of involvement of the axillary lymph nodes. The patient's temperature was 101° F., and the leukocyte count was 13,500 per cubic millimeter of blood. Other routine laboratory determinations did not disclose any abnormality.

It was believed that the patient had acute mastitis and an abscess of the breast. On the day after her admission, she was brought to the operating room for incision and drainage of the abscess. Incision produced a moderate amount of serosanguineous fluid. The mam-

FIGURE 1. Appearance of incised tumor in case 1.

mary gland seemed to be degenerated and friable. A specimen was removed for microscopic examination, and drainage was established. Microscopic examination of the specimen disclosed myxoid degeneration of the stroma. In the degenerated stroma there were a number of duct structures that were hyperplastic and lined with cuboidal and low columnar epithelial cells. There was a marked predominance of stromal elements, and broad areas of degeneration and necrosis were evident. The pathologic diagnosis was cystosarcoma phyllodes.

FIGURE 2. Surgical specimen in case 3.

Two days later, simple mastectomy was performed. The tumor (figure 1) contained masses of firm and soft gelatinous tissue. It measured 15 by 15 by 8 cm. and weighed 250 gm. It appeared nodular in some areas.

The patient was dismissed from the hospital a few days later, and her condition has remained satisfactory.

Case 2—A white married woman, aged 42 years, was admitted to the hospital because of a lump which had been present in the lower outer quadrant of the right breast for about two months. The lump was not painful. It was not attached to the skin, and there was no retraction of the nipple. Routine laboratory tests and roentgenographic examination of the chest did not reveal any abnormality.

Biopsy was performed. Actually, the entire lump was excised. It was white in color, oval, and measured about 4 by 4 cm. On cut section, the tumor was firm and had a gelatinous and myxoid appearance. Microscopic examination showed marked nuclear variation of the stromal element. In some areas, the cells were forming a moderate amount of collagen; in other areas, the stroma was myxomatous. The tumor did not have a distinct capsule, but it seemed to be fairly well demarcated. Pathologic diagnosis was cystosarcoma phyllodes.

Two days after the lump was excised, simple mastectomy was performed. The convalescence was uneventful, and the tumor has not recurred.

Case 3—A white married woman, aged 75 years, was admitted to the hospital because of a mass which had been present in the right breast for five years. The tumor was asymptomatic, and its size had remained almost constant for several years. Recently, however, the tumor had started to grow rapidly, and it had attained an impressive size in four months.

The right breast was bulky. The veins were dilated, and the breast was markedly discolored. A thick sanguineous discharge could be obtained by pressing the nipple. It was believed that the patient had an inoperable carcinoma of the breast. Biopsy was performed. A mass of hemorrhagic necrotic tissue meas-

uring 12 by 10 by 6 cm. (figure 2) was sent to the pathologic laboratory. Microscopic examination disclosed a tumor composed of differentiated breast stroma. It contained numerous elongated and dilated hyperplastic duct structures. There were broad areas in which hemorrhage, degeneration, hyalinization and cystic formation were evident. The pathologic diagnosis was cystosarcoma phyllodes.

Simple mastectomy was performed two days later. The convalescence was uneventful, and the tumor has not recurred.

Case 4—A white married woman, aged 42 years, was admitted to the hospital because of a lump which had been present in the right breast for at least five months. The lump was situated at the 3 o'clock position in the right breast. It was freely movable, and was about 3 by 4 cm. in size. A white round tumor was excised on April 18, 1957. It was well encapsulated, and was 3 cm. in diameter. Microscopic examination revealed areas of marked stromal overgrowth, myxoid changes of the stroma, and separation of the cell fibers by vacuolated intercellular material. Between the areas of dense cellularity, there were broad areas of partial hyalinization and collagenous deposition within the connective tissue. There was no evidence of local invasion. The pathologic diagnosis was cystosarcoma phyllodes.

The patient was dismissed on the third day after the operation. There has not been any recurrence of the tumor.

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Newer Developments in the Management of Early Prostatic Cancer

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Prostatic carcinoma is one of the most common neoplasms occurring in men.

Early diagnosis is important; a semiannual rectal examination, with biopsy of suspicious areas, is recommended for all men more than 50 years old.

Palliative therapy alone produces an average survival of only three or four years.

Treatment must be individualized. Combinations of surgery, hormonal manipulation and interstitial irradiation are effective.

Due to the high incidence of involvement of regional lymph nodes, lymphadenectomy is done in addition to radical prostatectomy in selected patients.

R. H. FLOCKS

CANCER of the prostate is a very common malignant disease which, in spite of previous advances in therapy, still carries a poor prognosis. Perhaps a great deal of the difficulty of increasing the cure rate of this tumor lies in the fact that in the majority of cases it arises in the outer portion of the prostate, producing symptoms of urinary obstruction or pain late in the course of the disease. In routine autopsies of men more than 40 years of age, Moore discovered that 21 per cent had cancer of the prostate gland which was not evident clinically. With the increasing age of our population, it becomes evident that this neoplasm is one of the most common occurring in men. In spite of the advances made in the treatment of this type of cancer over the past several decades, a review of 1300 patients treated at the University Hospitals, Iowa City, by palliative means and followed for five years or more revealed that the average survival of these patients was approximately three years. If one compares this survival with the life expectancy curve for men, it is seen that palliative therapy falls far short

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of providing these individuals with a survival anywhere near their expectancy.

A review of the literature and of our own experience indicates that it is extremely important to individualize the management of patients with prostatic cancer. The age, temperament, home environment, sexual status and general physical status of each individual patient must be considered when a course of management is outlined. It may well be that in selected individuals the age and condition may preclude radical surgery in a particularly suitable case; however, irradiation therapy plus hormonal environmental alteration may be of great help in controlling the neoplasm. After these factors have been considered, the stage of the pathologic process is significant.

Classification of Prostatic Cancer

The following groups of prostatic cancer have been delineated as a result of a study of 571 patients without clinical evidences of metastatic spread and a total of 1300 patients followed over five years at the University Hospitals, Iowa City.

Group 1—About 5 per cent of the total number of patients seen were in group 1. In this group, the lesion was completely limited to the prostate itself, and the patient was in good general condition so that surgery in the form of radical perineal or retropubic prostatectomy could be carried out. Usually, this lesion was found incidentally as a result of a general physical examination which included an adequate rectal examination.

Group 2—This group consisted of essentially 25 per cent of all the patients admitted to the University Hospitals with a diagnosis of prostatic cancer. In this group, the lesion was locally inoperable. It had spread beyond the confines of the prostate itself, had invaded the prostatic capsule, and had spread to the region of the base of the bladder or the region of the seminal vesicles. In some cases it had spread enough internally to involve the urethra and to obstruct the bladder neck. However, there was no evidence of any distant metastasis. The bones were negative, the acid and alkaline phosphatases of the serum were normal, and, on retropubic exploration, no evidence of regional lymph node involvement was found.

Group 3—This group included essentially those patients who had a lesion on rectal examination which was the same as that seen in patients in group 2. The general physical examination, the x-ray pictures of the bones, and the serum acid and alkaline phosphatases were also normal. The difference between the two groups was that retropubic exploration of patients in group 3 showed that pelvic lymph nodes were involved to a slight or marked degree by spread from the local tumor. These patients represented about 20 per cent of the total number studied.

Group 4—Patients who had a lesion which had spread away from the local area were designated as group 4. There was an elevation of the serum acid phosphatase in those patients who had not received estrogens or who had not had an orchiectomy. The local lesion was inoperable. There was evidence of spread to the bones, and retropubic exploration showed evidence of spread to the lymph nodes above the level of the bifurcation of the common iliac vessels. These patients made up approximately 45 per cent of the total number of patients seen at the University Hospitals, Iowa City.

Diagnosis and Treatment

As a result of our studies, we concluded that palliative therapy alone gives only an average survival of three years. This includes transurethral prostatic resection or suprapubic cystostomy to relieve obstruction of the bladder neck if it is present, orchiectomy and administration of estrogens to alter the hormonal environment of the tumor, and any other therapy which will make the patient more comfortable and tend to retard the growth of the neoplasm. Intravenously administered nitrogen mustard, for example, has been found to give some palliation in these advanced cases.

Since only a very small percentage of these cases (less than 5 per cent) are amenable to surgical removal of the entire lesion and since palliative therapy gives results which are very definitely limited in efficacy, it would seem

that more radical attempts to destroy the lesions of groups 2 and 3 are indicated.

Two new procedures have been added to the management of patients with prostatic cancer classified in groups 2 and 3. These are: (1) the institution of radiation therapy, utilizing the flexible properties of the radioisotope of Au^{198} to supplement destructive therapy of the lesion by surgery and cauterization, and (2) the recognition of the high incidence of regional lymph node involvement in patients who do not have any more distant spread. This recognition has resulted in the addition of lymphadenectomy to radical prostatectomy plus irradiation for localized prostatic cancer in selected patients in group 3.

The fact that palliative therapy for prostatic cancer has been unsatisfactory also has led to an improvement in the methods for early diagnosis. Routine rectal examination every six months of all men more than 50 years of age, with biopsy of any suspicious areas, is indicated. It is obvious that the earlier the lesion is discovered, the better will be the opportunity to destroy it by a combination of surgery and irradiation. Diagnostic procedures include transrectal needle biopsy and open perineal, open retropubic and transurethral biopsies. Of these, the least accurate is the transurethral method, because in 95 per cent of all cases the lesion begins in the posterior lobe. Open perineal biopsy is the most exact procedure, with the other two methods rated a close second and third. Transperineal needle biopsy is not nearly as accurate as transrectal needle biopsy, and at the University Hospitals it is used only in rare instances.

Having made a definite diagnosis of prostatic cancer, what is the next step in caring for the patient? The lesion is classified by a careful evaluation of the biopsy, rectal examination, serum acid and alkaline phosphatases, x-ray pictures of the bones (particularly of the pelvis), and results of a general physical examination. Intravenous pyelography is employed to see the extent of obstruction to the bladder neck or the ureters or both. If the general condition of the patient is good and the lesion is in group 1, as outlined in this report, radical prostatectomy by either the perineal or retropubic route is indicated. There is only a 7 per cent chance that the regional lymph nodes are involved, and there is at least a 60 to 70 per cent chance that a five year cure without evidence of local recurrence or dissemination will be achieved by an adequately performed radical prostatectomy by either route. There will be a small incidence of incontinence and, of course, total impotence in this situation. Depending on outside factors, hormonal manipulation can be added to this therapy if so desired.

If the lesion falls into group 2 or 3, an attempt to destroy the lesion with or without the addition of hormonal manipulation is indicated if the general condition of the patient will tolerate one or two comparatively minor surgical procedures. Destruction by irradiation of the lesion, utilizing either the open perineal, the transrectal or open suprapubic technics, should be carried out. If the lesion falls into group 3, with involvement of the pelvic lymph nodes, lymphadenectomy can also be carried out.

Results of Treatment

Since 1951, over 600 patients in groups 2 and 3 have been treated at the University Hospitals by a combination of interstitial irradiation with radioactive gold and lymphadenectomy, with or without the addition of hormonal manipulation. It is of interest to study the results obtained. Once it was recognized that problems of distribution could be at least practically solved by using a small volume with a large dosage of radiation and by repeated injections at two month intervals, satisfactory results could be obtained in the smaller groups of glands. When to this was added lymphadenectomy in patients in group 3, striking results were achieved in the smaller glands, without marked infiltration locally and without massive involvement of many of the regional lymph nodes.

The mortality and morbidity have been extremely low. In a recent study[1] only four hospital deaths were noted in over 785 procedures among 517 patients; only two of these appeared to be related to the procedure and

TABLE 1

COMPLICATIONS IN PATIENTS WITH PROSTATIC CARCINOMA[1]

COMPLICATIONS	PATIENTS			
	(1-50)		(50-517)	
	Number	*Per cent*	*Number*	*Per cent*
Rectal ulceration	8	16	2	0.5
Leukopenia	3	6	6	1.3
Calculus formation	1	2	14	3.1
Stricture of prostatic urethra	0	0	7	1.6

none were due to effects of radiation. The complications are enumerated in table 1. Rectal complications have disappeared with an understanding of the influence of volume and fascial planes on the spread of Au^{198} solution.

The results of five year follow-up studies in the first 135 patients (all of whom were clinically inoperable) are stated in table 2. Note the results in those patients with small glands in whom the problems of distribution could be overcome. It is also of interest that of the 32 patients with positive lymph nodes, four are clinically well at this time. Surgical removal combined with injection of Au^{198} in the areolar tissue might well have afforded a much better result in these patients.

It is interesting to compare the five year survival of a similar group of patients (same average age and with the same stage of disease when treatment was started) who were treated at the University Hospitals by palliative means (including endocrine control) with the five year survival of the patients who had interstitial irradiation. The survival rate was approximately 30 per cent for the first group and 42 per cent for the second, an improvement of approximately 33 per cent. Examples of the results of therapy are illustrated in the following case histories:

Case 1—A 66 year old man underwent a transurethral resection July 7, 1954 for prostatic carcinoma and urinary retention. On July 22, retropubic exposure of the prostate was carried out. No enlarged regional lymph nodes were found. The prostate was the seat of a large cancer that involved both lateral lobes, the anterior lobe, the subtrigonal area and both seminal vesicles. Induration was lateral from the prostate on each side. By sharp dissection, the prostate and as much as possible of the seminal vesicles, subtrigonal area and prostatic pedicles were removed. The pedicles and adjacent areas on each side were infiltrated with a total of 50 mc radiogold in

TABLE 2

FIVE YEAR SURVIVAL OF 135 PATIENTS WITH PROSTATIC CARCINOMA[1]

SIZE OF GLAND (GM.)	PATIENTS	NO CLINICAL EVIDENCE OF DISEASE	LOCAL RECURRENCE	METASTASES	PATIENTS ALIVE	
					Number	*Per cent*
Under 20	11	9	0	1	10	91
20-34	17	6	2	0	8	47
35-54	54	12	1	6	19	35
55-100	33	3	2	2	7	21
Over 100	20	2	0	0	2	10
TOTALS	135	32	5	9	46	34

3 cc. diluent. The postoperative course was uneventful. As of September 1959, the patient was well. Rectal palpation revealed nothing that might indicate neoplasm. Urination was satisfactory. No endocrine therapy was instituted. It is too early to state the ultimate result in this case, but the patient's condition was satisfactory 62 months after therapy.

Case 2—A 57 year old man was hospitalized on August 27, 1952. A large group 3 prostatic cancer with involvement of the local lymph nodes was found. The whole area was infiltrated with Au^{198} in three treatments. As of December 1959, no evidence of recurrence was found.

Case 3—An 80 year old man was admitted to the University Hospitals on October 30, 1950, with retention of urine due to a large prostatic carcinoma involving the base of the bladder and both seminal vesicles; it was fixed to the pelvic fascia. No bony metastases were seen. Transurethral prostatic resection was carried out and endocrine therapy instituted. The patient returned in one month with severe bladder irritation and gross hematuria. Secondary transurethral resections and coagulations and bladder irrigations yielded only temporary improvement. In spite of endocrine therapy no change occurred in the rectal findings. On March 23, 1951, this patient's difficulties were maximal, and 70 mc radiogold was infiltrated into the tumor. At the time of operation both seminal vesicles, both lateral lobes and periprostatic tissue on each side were involved. The lymph nodes could not be palpated. The patient improved steadily and by May 1951 was asymptomatic. On June 25, 1951, the rectal findings showed no definite tumor, and biopsy was negative for cancer. The patient had no further difficulty with his prostate or bladder. He died suddenly of a vascular accident in September 1953, having lived comfortably for two and one-half years after Au^{198} therapy. Rectal and x-ray examinations one month prior to death were essentially negative.

Summary

The points to be emphasized with regard to prostatic cancer are as follows:

1. Prostatic cancer is a common disease entity. Four stages may be recognized, the first three of which are amenable to attempts at destruction by surgery and the use of interstitial irradiation.

2. Palliative therapy, including all types of hormonal manipulation, has not produced cures. The average survival is three to four years.

3. Early diagnosis by frequent rectal examinations and adequate biopsy is worthwhile since early prostatic cancer can be treated by surgery or irradiation technics, utilizing the flexible properties of interstitial radiation with Au^{198}, or both.

4. Combinations of surgery, hormonal manipulation and interstitial irradiation are useful and not mutually exclusive.

5. Removal of regional lymph nodes may add much to the prognosis in the individual patient.

REFERENCE

1. Flocks, R. H., Culp, D. A. and Elkins, H. B.: Present status of radioactive gold therapy of prostatic cancer. J. Urol. 81:178 (January) 1959.

SYMPOSIUM

Evaluation of the Acute Abdomen

ROBERT M. ZOLLINGER,[1] WALTER G. MADDOCK[2] AND STEWART WOLF[3]

Some of the subjects covered in this panel discussion on evaluation of the acute abdomen are the pain mechanisms involved, the importance of a knowledge of anatomy, the significance of boardlike rigidity, the physical examination, laboratory studies in diagnosis and in analysis of clinical findings, information to be gained from roentgenologic studies, significance of shock, and important considerations in differential diagnosis of surgical and nonsurgical conditions.

ROBERT M. ZOLLINGER

DR. ROBERT M. ZOLLINGER (Moderator): We have always considered the acute abdomen as more or less of a surgical emergency and we think we do a pretty good job in evaluating these cases, but we know there is always room for improvement. We hope we can clarify some of the problems that may be encountered.

Dr. Maddock, how important is it to listen to the patient's story? Is there still a place in these modern days for history taking?

DR. WALTER G. MADDOCK: Of course one must get a good story from the patient as to what is going on. The patient can often tell you important details leading to the proper diagnosis. Just recently I saw a patient who had been treated in the hospital for intestinal obstruction. There was some abdominal distention present. A flat plate of the abdomen showed distended loops of small bowel. The patient had not had a previous operation. A background for obstruction of the small bowel was not present. I asked the patient how his illness began, and he said he first had some nausea, that he vomited once, and that he had had some generalized abdominal pain and now it seemed to be over in the right side. One really would need nothing more to make a

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diagnosis of appendicitis. That is a good example of what one can learn by asking the patient about his illness, and it will work out this way in a great many cases.

Mechanisms of Pain

DR. ZOLLINGER: Dr. Wolf has been the leading authority on the analysis and study of pain and has made many contributions in this field, and I am going to ask him to talk about the pain mechanisms involved in the acute abdomen.

DR. STEWART WOLF: Briefly, I would like to make three points. First, abdominal pain implies the activation of pain mechanisms which are carried in pathways that are well defined if not actually understood. These pathways, we know, have a segmental distribution. A large number of segments may be involved and still produce pain in the abdomen, including some cervical segments that innervate the diaphragm—C3, C4 and C5, and including, of course, all the thoracic segments down to T12. Second, it is odd and interesting that often the pain is not felt throughout the segment, so that relatively few pains are girdle-type pains; they are more likely to be felt in the anterior portion of a segment. The pain of ureteral colic, for example, usually is felt more anteriorly than posteriorly. Third, and this is perhaps the most complex aspect of pain mechanisms, deep pain differs from superficial cutaneous pain in a very interesting way, and that is that it is inclined to be referred. Referred pain means pain that is felt at a site other than the one where the stimulation is occurring. Other aspects of referred pain include superficial hypalgesia of the skin, tenderness in the muscles and deep tissues, and stiffness of muscles. The mechanisms responsible for referral of deep pain, including visceral pain, are not fully understood, but I would like to give a possible explanation of the phenomenon of deep pain.

A point that we often forget is that nerve fibers which carry visceral pain and travel in the sympathetic chains have their cell bodies in the same place as do intercostal afferents, and there is no essential difference between visceral and somatic afferents as far as distribution of cell bodies is concerned. There is no such thing as an autonomic sensory nerve; all autonomic nerves are efferent. The sympathetic chains simply serve as conduits for the visceral afferents, and all the cell bodies of the afferents are in the dorsal root ganglions.

Let us assume that there is an adequate stimulus in the stomach and the excitation travels in the visceral afferent in a sympathetic chain with its cell body in the dorsal root ganglion. It sets up an area of excitation in the dorsal root. The phenomenon of referred pain can be explained as follows. One may have a pain at some distance from the original site of stimulation. The spread of excitation catches not only the secondary fiber at that segment but also spreads headward and tailward to catch the secondary afferents of neighboring segments and also spreads to some extent across the cord, so that one may feel pain in the opposite side of the body.

Not only are the secondary afferents of the same segment and of neighboring segments and across the cord sometimes involved in the spread of excitation set up by the original afferent stimulus, but other afferent nerves coming in over these same pathways may be caught up in this electric spread. Afferents from the skin may be involved and tenderness may develop. Afferents from deep muscles are caught up, and the muscles become tender.

There is an efferent side to referred pain as well. The spread of excitation extending downward near the lateral horn where the autonomic fibers, the sympathetic fibers, take their origin may give rise to secondary effects in blood vessels, glands, and so on, because the sympathetic cell is caught up in this spread of

excitation set up originally by the afferents.

In addition, skeletal muscles may be involved in referred pain because the internuncial neuron which comes down from the dorsal horn to the ventral horn is again caught up in this wave of excitation, the anterior horn cell is activated, and out goes an impulse to a skeletal muscle—making the neck of the person with meningitis stiff, making the abdomen of the patient with intraabdominal disease stiff. But, and this is extremely important, this tight muscle at the end of the story may in turn become a source of pain; indeed, in renal colic some of the pain comes from the ureter and some comes from the intensely sustained contractions of the back muscles. If such a muscle becomes the secondary source of deep pain, the entire cycle can be repeated again, and it is apparent how the pain ultimately may be felt some distance from the original site of stimulation.

Anatomic Considerations

DR. ZOLLINGER: Dr. Maddock, in the old days one could not be a surgeon without studying a lot of anatomy. Does it help to restudy anatomy once in a while?

DR. MADDOCK: There is no doubt that a knowledge of anatomy plays an important part in the surgeon's skill and is often an aid in the diagnosis of the acute abdomen. For instance, it took me quite a bit of time to realize that in palpating the right lower quadrant I had to get away from thinking of it simply as an area and instead to think about what was underneath anatomically. Again, in the right upper quadrant there are many structures that one actually puts pressure on in palpation, so a knowledge of anatomy is quite necessary. There are other anatomic facts that will help in understanding the spread of disease in the acute abdomen. For example, a perforated ulcer allows fluid to spread down the right pericolic gutter and to produce many of the most severe findings in the right lower quadrant. Similarly, the ascent of fluid from a ruptured appendix up to the subdiaphragmatic spaces is important, and it is necessary to know the anatomic locations there of the suprahepatic and infrahepatic spaces, and whether an abscess is posterior or anterior to the triangular ligament so that one will know where to make the approach to provide proper drainage. Anatomy is still an important part of a surgeon's skill.

DR. ZOLLINGER: Do you think we tend to forget the function of the various gutters in directing fluid from the upper abdomen to the lower abdomen?

DR. MADDOCK: We must keep the various anatomic pathways in mind all the time. As I said, fluid coming up from the pelvis along the right side tends to rise not in the midline around the small intestine but laterally along the colon.

DR. ZOLLINGER: What if you have a patient with pain in the left upper quadrant? Do you take that a little more seriously?

DR. MADDOCK: From a diagnostic standpoint, pain in the left upper quadrant is a little more disturbing. The spleen generally is not a common cause of pain in the acute abdomen, but the pancreas can produce severe acute abdominal pain.

DR. ZOLLINGER: If you own the old Kelly textbook or can get hold of it, I recommend that you read it again. It is beautifully illustrated and very worthwhile. It points out the location of the appendix in the pelvis and how one can overlook the classic pain over McBurney's point just because of normal anatomic variation.

DR. MADDOCK: Another point of occasional interest is the manner in which the sigmoid can roam pretty well across the abdomen and be over on the right side, so a diverticulitis of the sigmoid can produce most of the symptoms in the right lower quadrant normally regarded as being those of appendicitis.

DR. ZOLLINGER: We suggest you rush home and read a little bit of anatomy.

Boardlike Rigidity

Dr. Wolf, what about the boardlike abdomen? If I see a patient with a boardlike abdomen, I tend to believe it is a surgical situation. Would you disagree?

DR. WOLF: No; it is very likely to be a surgical situation. However, "a boardlike abdomen" is a relative term, and I am not certain

everyone in this room would define it in the same way. I believe that the muscle tightness, which, of course, is responsible for the rigidity —and which, as I pointed out, may itself be a source of pain—depends on the efferent limb of the referred-pain phenomenon, and it seems to be proportional to the intensity of the original afferent pain stimulus. The more intense the pain stimulus that comes into the spinal cord at the dorsal horn area, the greater is the spread of excitation and the degree of excitation within the cord, and the larger the number of impulses that are fed into the anterior horn cells which go out to the muscles of the abdomen and cover the whole thoracic segmental distribution.

DR. ZOLLINGER: Wouldn't it be necessary for a coliclike pain, then, of that type to be present to produce boardlike rigidity without peritonitis, for example?

DR. WOLF: Boardlike rigidity would almost certainly imply peritonitis, but not necessarily surgical in the sense that operation should be performed.

DR. ZOLLINGER: Name one situation that would not be surgical in that sense.

DR. WOLF: I was thinking of acute pancreatitis.

DR. ZOLLINGER: That's right; that would be one. Tell me, do you ever see unilateral boardlike rigidity? Can it be present on one side or the other in referred pain?

DR. WOLF: No, I would not describe that as boardlike rigidity, although I have heard it called that. I think boardlike rigidity simply means a very tight, tense abdomen that feels as hard as a board, and the term usually is reserved for bilateral tightness.

DR. ZOLLINGER: You would feel better, therefore, if a surgeon was looking after you rather than somebody else if you had a boardlike abdomen?

DR. WOLF: If I had an abdominal pain I would like to have a surgeon as well as an internist looking after me.

DR. ZOLLINGER: Dr. Maddock, if you have a patient with a boardlike abdomen, are you going to call in a lot of extra help?

DR. MADDOCK: Most of the time when I see a patient with a boardlike abdomen a medical man has referred him to me, so an internist is on the job in the first place. But I agree with what has been said. With boardlike rigidity the chances are good that a surgical lesion is present that is going to require operation, and one had better be sure of the situation to treat it conservatively. In considering operation I think one has to bear in mind the percentages, as one does in handling any disease. There may be confusing findings, but with a boardlike abdomen the onus is going to be on the surgeon if he does not operate. It is most distressing if it is found at autopsy that a patient had a surgical lesion that could have been treated.

DR. ZOLLINGER: How many of the physicians in our audience would recommend surgery, by and large, for a boardlike abdomen? (A majority.) How many would call in help and cogitate about it for a while? (Only a sprinkling of hands.)

Examination of the Patient

Dr. Maddock, how do you examine a patient with acute abdomen, and does the age of the patient influence you? I remember the story about the way Reginald Fitz would walk into the room of a youngster and tell the child to cough and then to sit up; if the patient had no pain when he coughed or when he sat up, Dr. Fitz would not take too seriously the possibility that the youngster had appendicitis. How do you examine these patients?

DR. MADDOCK: I always remember the time when I was a resident and I called my chief, Dr. Hugh Cabot, to come and see a youngster of four in the hospital with a questioned acute appendicitis. It was 4 o'clock in the morning when I got the chief out of bed. He came into the room, looked at the youngster, who was sleeping, and said, "This is not appendicitis. A child will not sleep with appendicitis." Then he left. I had quite a time convincing the child's parents that Dr. Cabot was an expert and did not need to examine the patient to make the diagnosis. The chief happened to be right, but I would not recommend his method.

The best method is a systematic routine examination of the abdomen, with inspection of the whole patient to see whether he is ap-

prehensive or taking it easy (which is going to change your estimation of some of the signs), examination of the belly with a good light, and then palpation, not approaching the sore spot first. These are all routine, simple things. Also important are auscultation of the abdomen and percussion. One gets the most information by following the routine procedures. It is difficult to put this across to the medical students, because they soon want to shorten histories and physicals; but the fundamentals of examining a patient still serve us very well.

DR. ZOLLINGER: Dr. Wolf, have you any diagnostic nuggets to offer in regard to this examination?

DR. WOLF: I agree with everything Dr. Maddock said. One very useful item, very often, is an attempt to estimate the intensity of the pain. This is difficult but is immensely important in the analysis of the clinical problem. One way to do it is to squeeze the biceps muscle between your thumb and forefinger as hard as you can. This will induce pain of an intensity of a little more than 50 per cent, based on the intensity range beyond which further stimulation will not increase the sensation.

DR. ZOLLINGER: Say that again. I am squeezing my biceps and I don't receive any message from that.

DR. WOLF: It is always possible to squeeze someone else's biceps harder than your own.

DR. ZOLLINGER: Obviously he is a professional pincher.

DR. WOLF: What I mean is that if you squeeze the biceps as hard as you can and the patient says, "Oh, this pain is much more intense than the abdominal pain," you know the latter pain is not of very high intensity. On the other hand, if such a squeeze brings the response, "Oh, this pain is peanuts compared with the abdominal pain," you know the patient does have a high-intensity pain. I think this estimation of pain intensity is very important, because the amount of anguish or complaint the patient manifests is not at all proportional to intensity.

DR. ZOLLINGER: That is a good point. Dr. Maddock, do you have any tricks like that to judge the severity of pain?

DR. MADDOCK: I have mentioned that one should assess the whole patient and judge the response activity—whether he is lethargic, active, writhing; whether you think he is putting on more of a show than he should in relation to the abdominal pain. All these are points by which one is going to judge the intensity of the pain in the belly.

I remember once during World War II when I was making rounds with a brigadier general in England and we saw a patient suddenly go into a spasm and turn on his side and writhe with "abdominal pain." The general said, "It is the first time in my life I ever saw an ulcer perforate right under my eyes." About a half-hour later, when the inspection was over, he said, "Now, we'll go back and see that perforated ulcer." The soldier was reading a newspaper.

Laboratory Aids in Diagnosis

DR. ZOLLINGER: These days everybody in universities is accustomed to overdoing the laboratory work. I have heard it said that when a fellow gets out of medical school today all he can do is depend on laboratory work and instruments. Dr. Wolf, what about laboratory methods?

DR. WOLF: The point you made about undue reliance on laboratory data is very important. After all, diagnosis depends on analysis of a clinical problem, not on criteria. Many medical schools make the mistake of teaching differential diagnosis in terms of criteria, for example, that multiple sclerosis depends on three criteria that Charcot outlined; these may all be absent in a case of multiple sclerosis. The important thing is to be aware of the nerve pathways and the indicators of involvement of these nerve pathways in the whole complete examination, as Dr. Maddock said. In the analysis of a clinical problem, criteria such as white blood cell counts and other types of blood studies actually may be misleading. It is well known, for instance, that pain itself and emotional stress may lead to an increased white blood cell count.

DR. ZOLLINGER: How much?

DR. WOLF: There is some disagreement on this point, but I would say up to about 18,000.

In my experience I am reasonably satisfied with about 16,000 to 18,000, but I would not put an upper limit on it, because the more we learn about the way the higher neural centers can enter into bodily mechanisms, the more respect we have for them. But in any case, a person may have inflammatory disease in a viscus without having an elevated white blood cell count.

There are certain laboratory studies which are very important in directing attention toward what one might call a medical disease rather than a surgical explanation of severe abdominal pain. One, of course, would be a test for sickling in the blood. It has not been at all uncommon for patients with sickle-cell anemia in crisis to be operated on, and this perhaps could have been avoided by doing a sickling test. A high index of suspicion and a careful history will lead one to make the proper studies; one cannot do all the tests on every patient.

DR. ZOLLINGER: Suppose that tonight after you return home the president of the university is brought to the hospital with an acute abdomen. What tests would you want?

DR. WOLF: I would not rely on one test or a series of tests to make the diagnosis. I would, first of all, not be in a great hurry. I know that internists are accused of moving slowly, but I think lots of times one avoids difficulty by not considering everything that is very uncomfortable as being an emergency.

DR. ZOLLINGER: But this is rather urgent. What laboratory test do you want?

DR. WOLF: I would certainly want a white cell count.

DR. ZOLLINGER: Would you examine the urine?

DR. WOLF: I would certainly want a urinalysis done.

DR. ZOLLINGER: How much more?

DR. WOLF: Probably I would want a blood amylase.

DR. ZOLLINGER: A blood amylase. What is your thinking of the president of the university and what he has been doing?

DR. WOLF: Nowadays it is necessary for university presidents to raise a lot of money, and to do this it is necessary to go to a good many gatherings. Sometimes gatherings pile up.

DR. ZOLLINGER: Well, then, you would depend on an amylase determination and you would wait an hour or two between intervals. Would you want the white blood cell count repeated, say, in three or four hours?

DR. WOLF: I cannot say that I would follow any routine procedure. What I did would depend on my suspicions, and I would not use any specific set of rules or criteria.

DR. ZOLLINGER: Would you obtain a blood amylase determination routinely on patients with acute abdominal complaints unless you thought they were typical of appendicitis?

DR. WOLF: No.

DR. ZOLLINGER: How do you feel about this, Dr. Maddock?

DR. MADDOCK: I wouldn't order a blood amylase determination for a patient if I thought he had acute gallbladder involvement or if I was pretty sure he had a ruptured ulcer or acute appendicitis, but if the diagnosis was a little more difficult I certainly would use the amylase.

DR. ZOLLINGER: I consider the amylase invaluable. It has saved me from difficulty perhaps just as much as the white cell count. I think we tend to depend on the amylase right along with the white blood cell count.

DR. MADDOCK: I left a lot of leeway for your amylase test; I took only three diseases away.

DR. ZOLLINGER: And gave me a chance to say a few words; thank you.

Dr. Maddock, what about the white blood cell count? Some of the literature indicates that in acute appendicitis perhaps it isn't so necessary. How much do you really use it now? Dr. Wolf said that if a person gets excited the count will go to 18,000.

DR. MADDOCK: I think one has to use the white blood cell count along with the general review of the patient—the whole picture. In appendicitis the white blood cell count follows a fairly common pattern in a good many cases —about half of them—and will be within a range of 12,000 to 13,000. But every one of us has seen cases in which the white blood cell count was normal in the presence of acute appendicitis, and conversely we have seen patients with very few signs of right lower quadrant

tenderness and muscle spasm with counts of 20,000 or 25,000; so here again one has to use clinical judgment. The white blood cell count is one of the factors to evaluate along with the others.

DR. ZOLLINGER: Of course if one finds a count of 20,000 or more, one is a little more concerned than if it were 8000 or 10,000. Isn't that right?

DR. MADDOCK: Yes. I am sure one cannot ignore this. I happened to be looking through a British surgical journal recently and found a statement that the white blood cell count can mislead the most astute clinician and therefore should be disregarded. That is a very unusual statement in a textbook prepared for students, and I would not agree with it at all. We must know about the white blood cell count. We must know its variations and talk about its variations to students and not ignore it, any more than we would ignore the variations in right lower quadrant tenderness and muscle spasm in appendicitis.

DR. ZOLLINGER: Dr. Wolf, what is your feeling about the white blood cell count in acute appendicitis?

DR. WOLF: I agree completely with what Dr. Maddock said, and would like to make another point about diagnosis. It seems to me that often the most productive thing in the analysis of a case is something that doesn't fit. So often, practicing medicine is compared to repairing an automobile, and the doctor is made analogous to the garage mechanic; there is something wrong with the car, so you take it to the garage, where the mechanic figures out the trouble and puts it right. We understand exactly how a car operates, and we understand the principle of the internal combustion engine, but we understand only a small part of the operation of the human body. Doctoring, therefore, is in reality far more analogous to detective work. One cannot give a detective six criteria for an inside job and six criteria for an outside and six others to tell him that the butler did it; he has to take all the data and analyze them, and often he gets a lead in the right direction by following the clue that doesn't fit. I think the same is true in diagnosis of acute abdomen. If something in the picture doesn't fit the diagnosis that seems obvious, it probably is the most important thing.

DR. ZOLLINGER: Of course the implication here is that if one is an internist one is more apt to find that by slow, prolonged deliberation. I am not so sure what Dr. Wolf just said is right, but it is a very good point. If it doesn't fit, one had better procrastinate a little bit and think over and search over. Not everything fits the book. How many doctors in the audience use a white blood cell count pretty much in appendicitis? (Majority.) How many do not? (About a dozen hands.) How many feel that a white cell count under 10,000 is not too important in appendicitis? (About 100 hands.) The majority are going to want the level to be higher than that to be significant.

Abdominal Pain Associated With Intrathoracic Conditions

Dr. Wolf, we were taught that one should not operate on a youngster with appendicitis until one had a chest plate, because of the danger of pneumonia. What about the diaphragm?

DR. WOLF: Intrathoracic diseases that may give rise to pain in the abdomen must be kept in mind, particularly rheumatic fever, lobar pneumonia and coronary occlusion. More often than not in these instances the abdominal pain is the result of some involvement of the diaphragmatic surface. This aspect of diagnosis is much more important in children than in adults, I believe, and certainly the patient's age is very important in evaluating pain and intraabdominal or indeed intrathoracic diseases. In old persons, for example, there may be very serious intraabdominal disturbance, including peritonitis, without any substantial pain. The diaphragm must enter into the analysis, and one must ask oneself whether there are evidences in the history or in the physical findings which would lead one to think in terms of intrathoracic disease—as I said, particularly rheumatic fever, coronary occlusion or lobar pneumonia. This, of course, implies examining the chest; and when the president of the university is brought in—and I hope he is not—the important thing will not be just to feel his belly and listen to it.

DR. ZOLLINGER: You mean you are going to examine his chest?

DR. WOLF: Yes.

DR. ZOLLINGER: How often have you been trapped, Dr. Maddock? Dr. Wolf touched a sore spot when he mentioned rheumatic fever, and I suspect there is a spy on my house staff, because not long ago I did take out an appendix in a youngster who did have, I think, rheumatic fever. Dr. Maddock, how many times have you been trapped by something in the chest, say a pneumonia, a collection of fluid, or infarction, and you thought the patient had appendicitis?

DR. MADDOCK: I see a patient occasionally with an infarct who has very distinct abdominal pain, but I haven't been trapped since I was a young instructor and operated on a youngster for appendicitis when he had pneumonia. I should have known better, because the white blood cell count was 35,000 at the time, which was a good lead. Once is enough to make a mistake like that.

X-rays

DR. ZOLLINGER: Do you use x-rays routinely in cases of the acute abdomen?

DR. MADDOCK: An x-ray of the abdomen is a very good source of information. It is not as important as an x-ray of the chest for the average patient coming in, certainly, but for the patient with acute abdomen one can get a tremendous amount of information from a flat plate. If gallstones are present, they show up in 30 to 40 per cent of flat plates; kidney stones appear in about 75 per cent if present. One gets a good idea about distention, whether it involves the small intestine, and what areas of the small intestine; one can get a pretty good idea whether there is complete or incomplete obstruction, which is a most important decision because the mortality for the former is about 30 per cent compared with 3 per cent for the latter. Air under the diaphragm is important; it shows up in about one-third of the cases of perforated duodenal ulcer in three hours, and in about two-thirds in six hours. The films that are of value here are a flat film with the patient supine and then an upright and a lateral projection to show air accumulating on the sides. One can get an impression of the vessels and calcifications here and there; maybe the splenic artery and other arteries will be visualized. Air in the biliary tree will be evident. A tremendous amount of valuable information can be gained from a flat plate of the abdomen.

One can go a bit further in regard to acute abdomen and x-rays. What about a careful barium enema? There may be colonic obstruction, and the problem can be discussed with the radiologist and a barium enema given without too much pressure to determine right away whether or not there is obstruction in the colon. Sometimes an intravenous pyelogram, made without preparation, will be of value in a case of acute abdomen in which disease is suspected in the kidneys. In general, our radiologic friends can give us a great deal of information in many cases of acute abdomen.

Shock Due to Overwhelming Infection

DR. ZOLLINGER: What is the significance of shock in a patient who has an acute abdomen, Dr. Wolf?

DR. WOLF: Usually shock implies a ruptured viscus, but it also may result from an overwhelming infection, particularly with gram-negative coliform organisms. A great deal of emphasis has been placed on this in recent literature. The evidence of infection that we depend on may be absent, including fever, even elevation of the leukocyte count, but nevertheless the presence of infection is important. Pyelonephritis would be one of the most common types, because this is the site where gram-negative organisms are very likely to live; and septicemia can produce gram-negative shock.

DR. ZOLLINGER: Do you think we miss a good many cases of infection today?

DR. WOLF: I am afraid we do.

DR. MADDOCK: I think that is true. I would like to say a word or two about a case I missed recently. Dr. Wolf referred to this type of situation, an instance of acute pyelonephritis with septicemia and then signs of peritonitis, abdominal muscular spasm, and rigidity with its origin seemingly in the pelvis. Two days

earlier, cystoscopic and sigmoidoscopic examinations had been made, and that brought up the question of perforation of either the bladder or the sigmoid as the cause of the whole picture and the shock. I operated on the patient. There was a small amount of foul-smelling pus in the abdomen. The autopsy diagnosis was acute necrotizing pyelonephritis. The blood cultures had been negative beforehand, but the cultures of the kidney were positive for coliform organisms.

Peritoneal Tap

DR. ZOLLINGER: Why didn't you do a peritoneal tap and study the fluid aspirated?

DR. MADDOCK: I thought of that afterward, but then I got only a small amount of fluid, 3 oz., deep in the pelvis; I doubt if a peritoneal tap would have reached this area.

DR. ZOLLINGER: Do you use peritoneal tap at all, or are you afraid to do it?

DR. MADDOCK: I use it once in a while, but I am not an enthusiastic advocate of the procedure. It may give some information in a difficult case, but I do not believe it is necessary in every case of acute abdomen.

DR. ZOLLINGER: Do you use it, Dr. Wolf?

DR. WOLF: Our surgeons sometimes do. The internists in our hospitals do not perform peritoneal taps. I think it can be valuable, but the thing we have to be careful about is that it doesn't get too fashionable so that people start relying on procedures rather than using the computer machine they have under their hair.

DR. MADDOCK: He means clinical judgment.

DR. ZOLLINGER: Obviously he is throwing the ball back to me. We have been using peritoneal tap. Our young men especially like it. I have never seen any harm come from it when it was performed properly, and I think it has helped us in many instances, especially in the differential diagnosis of acute pancreatitis and duodenal ulcer. A few of the boys, if they can get some fluid, will study the fluid for fat droplets, and check for the presence of bile or free hydrochloric acid. I think peritoneal tap has been of help to us in a few cases. However, in the diagnosis of hemorrhage in the abdomen we have had a number of cases in which a liter or more of blood was in the peritoneal cavity and yet a tap did not yield anything. The tap must be positive to be significant. A negative tap means nothing.

Differentiation of Mittelschmerz and Appendicitis

Dr. Maddock, how do you evaluate a case of a 17 year old girl who is sent in on the fourteenth day of her menstrual cycle with acute appendicitis? In three or four sentences, tell us how to tell the difference between mittelschmerz and appendicitis.

DR. MADDOCK: This is a difficult situation and one that leads all of us astray once in a while. I have probably done 20 or 30 appendectomies in my lifetime on such patients. Generally you find the patient was in an intermenstrual phase.

DR. ZOLLINGER: Fourteenth day.

DR. MADDOCK: Yes. The pain often begins acutely. Sometimes you get a story that the patient was running upstairs or there was some other special activity when the pain began. Usually she is not as sick as the patient with appendicitis, but again this may be a difficult differentiation.

DR. ZOLLINGER: You view it with alarm and have nothing to suggest to help, is that it?

DR. MADDOCK: Zollie makes it tough, but he knows as well as I that the differentiation between appendicitis and mittelschmerz is often difficult. However, if you make this mistake and take out a normal appendix, you are little to blame, despite the Tissue Committee.

DR. ZOLLINGER: I was about to ask about the Tissue Committee; this is Chicago, where it all started.

Dr. Wolf, there is McBurney's point and I thought there was an ovarian line that bisected at right angles Poupart's ligament. Am I wrong?

DR. WOLF: I am sure you are right about the emphasis on this; I question whether this holds up too well.

DR. ZOLLINGER: You don't believe a word of it, is that it? I think we have taken care of the ovarian line. I will go home feeling that we will continue to make the same old mistake and there is no foolproof way to distinguish between mittelschmerz and appendicitis.

Coronary Thrombosis as a Cause of Abdominal Pain

How about coronary thrombosis, Dr. Wolf? Can you always keep the surgeon from operating on a patient with pain in the abdomen?

DR. WOLF: Coronary thrombosis is an extremely important condition to keep in mind in the presence of intense abdominal pain, and again I would say that we often are inclined to think a situation is an emergency when this may not necessarily be the case. Certainly there are very definite emergencies in medicine, but the older we get the fewer times we feel a situation is actually an emergency. Coronary thrombosis represents the situation in which observation of the patient and careful evaluation of the problem often will protect the patient from operation.

DR. ZOLLINGER: If one is going to have abdominal pain with a coronary, where is it most likely to be located and what is it most likely to mimic?

DR. WOLF: It is most likely to be epigastric.

DR. ZOLLINGER: So it might be confused with colitis or pancreatitis?

DR. WOLF: Yes, or perforated ulcer. But I have seen pain of coronary occlusion down near the twelfth thoracic segment in the region of Poupart's ligament. One nugget of information here is that if the pain is in the neck, this doesn't fit the picture of abdominal disease. If the pain radiates up into the jaw, in the neighborhood of the neck, this is not acute abdomen, but it does fit the picture of a coronary. This is one of the few really reliable rules of thumb in evaluating abdominal pain.

Scheduling of the Operation

DR. ZOLLINGER: Dr. Wolf has implied that we should not be in too big a hurry to take care of emergencies at night. We have often wondered about that ourselves. Suppose a patient is brought in at night with an acute abdomen and the operative schedule for the next day is full. One has to try to arrive at a decision, because if operation is not performed at 11 or at 1 o'clock the patient may not be able to reach the operating room until the next afternoon. Dr. Maddock, how do you handle such a situation? Are you conservative?

DR. MADDOCK: We handle the situation exactly as you said, by being conservative. One doesn't want an overenthusiastic surgeon who goes for the knife as soon as the patient enters the hospital. I want to be conservative. Another factor here is the absence of the daytime hospital personnel.

DR. ZOLLINGER: We are going to end up here and ask you to be a little more conservative at night and wait. I think it is perfectly true that many decisions are made under the urgency of a full schedule the next day; and the personnel might leave something to be desired.

How many cases of acute appendicitis do you think have been held over from 1 o'clock in the morning until later that morning or early afternoon, Dr. Maddock, and have had a serious complication as a result of this delay? Would you testify against me if I made a patient wait in the hospital six hours with acute appendicitis?

DR. MADDOCK: I still stick to the rule that when you diagnose acute appendicitis that is the time to get the operation under way.

DR. ZOLLINGER: Dr. Wolf, what are you going to do?

DR. WOLF: This line of discussion isn't precisely my field, but I think there are fewer problems from waiting if a careful analysis is made. I might say that often in an accident situation in the emergency room the thing that is missing is the history, and it needn't be missing very often. The patient is uncomfortable and doesn't want to talk, but nevertheless usually the No. 1 kind of information is obtained from history, No. 2 from examination, and No. 3 from supplementary tests; and if you are going to make a diagnosis without No. 1, you are in an awkward spot.

DR. MADDOCK: I want to repeat the statement I made before, that when I have made a diagnosis of acute appendicitis, that is the time to plan for operation—right away.

Conclusion

DR. ZOLLINGER: To conclude this discussion, what can you tell us that will be helpful? Dr. Maddock, you are a teacher of surgery. You

have a group of boys who want some help from you. What test have you found most useful in diagnosis of acute abdomen? In other words, what have those gray hairs taught you?

DR. MADDOCK: Well, probably they have taught me to be conservative and look at the whole picture and get all the information that I can reasonably put together, and not be a knife-happy surgeon. I need to know all I can about the patient, have a complete history, get the results from a complete physical examination, call for all the laboratory studies that are indicated, and from these try to make the right diagnosis and employ the right treatment.

DR. ZOLLINGER: In other words, the older you get, the more pride you have in the accuracy of your diagnosis.

DR. MADDOCK: Of course; I hate to get caught, because my residents are going to razz me about my errors.

DR. ZOLLINGER: Dr. Wolf, give us a final statement.

DR. WOLF: Briefly, if one can figure out what it is that is hurting and can determine the mechanism of the pain, this can be enormously helpful, and to do this it is necessary to keep in mind what things can hurt. Distention and displacement of pain-sensitive blood vessels may give rise to pain. Sustained contraction of muscles, both smooth and skeletal, may give rise to pain. Relative ischemia of muscles can give rise to pain. I didn't mention abdominal angina, but this is another abdominal pain that may be very intense in association with exercise, owing to ischemia of the muscular structures in the belly. Unusually vigorous contraction or distention of muscles, both the tube muscles and the nontube muscles, may give rise to pain. Pulling, pinching or displacement of connective tissue may cause pain. Finally, inflammation of serous cavities may itself give rise to pain, but an inflammatory reaction or hyperemia in any body structure, including the mucosal lining of the stomach, may lower the threshold of pain so that ordinarily innocuous stimuli become painful.

DR. ZOLLINGER: What book would you recommend to help us to be better diagnosticians as far as the acute abdomen is concerned?

DR. WOLF: I think Zacchary Cope.

DR. MADDOCK: There is a recent book by Sherman Mellinkoff on the "Differential Diagnosis of Abdominal Pain" which is very good.

DR. ZOLLINGER: I want to thank Drs. Maddock and Wolf for their participation in this panel discussion. I hope it has proved helpful to all of us.

MEETINGS *and Postgraduate Courses*

AMERICAN COLLEGE OF GASTROENTEROLOGY, PHILADELPHIA: Annual postgraduate course in gastroenterology to be given at the Bellevue-Stratford Hotel, October 27-29. For further information, write to: American College of Gastroenterology, 33 West 60th Street, New York 23.

AMERICAN COLLEGE OF SURGEONS: Meetings to be held during 1961:

Sectional meetings:
Birmingham, Alabama, January 16-18
Mexico City, Mexico, January 23-26
Surgeons and graduate nurses, Philadelphia, March 6-9
Winnipeg, Canada, April 6-8
Annual clinical congress, Chicago, October 2-6

For further information, write to: Dr. William E. Adams, Secretary, American College of Surgeons, 40 East Erie Street, Chicago 11.

TENTH PACIFIC SCIENCE CONGRESS, HONOLULU: To be held at the University of Hawaii, August 21 to September 6, 1961, under the sponsorship of the National Academy of Sciences and the Bernice P. Bishop Museum. For further information, write to: Secretary-General, Tenth Pacific Science Congress, Bernice P. Bishop Museum, Honolulu 17, Hawaii.

CLINICAL STUDY

Trifluprομazine as a Potent Antiemetic Agent in Vomiting Due to Drug Toxicity

ARTHUR STEINBERG*

Albert Einstein Medical Center (Southern Division), Philadelphia

In 28 of 29 cases of nausea and vomiting, trifluprομazine proved superior as an antiemetic agent to chlorpromazine or dimenhydrinate. Vomiting was due to drug toxicity in 15 cases, nitrogen mustard being the principal causative agent; other immediate causes of vomiting included jaundice, cerebellar metastases, migraine, radiation sickness and gastritis. It appears that trifluprομazine is a highly effective agent in the elimination and prevention of nausea and vomiting.

ARTHUR STEINBERG

TRIFLUPROMAZINE hydrochloride (VESPRIN®), a trifluoromethyl phenothiazine derivative, has been shown to possess the versatility in clinical application characteristic of the phenothiazine family. It has been used effectively in the management of certain psychotic patients,[1-3] in the control of withdrawal symptoms in alcoholic patients,[4] and in the treatment of nausea and vomiting of varied causes.[5,6] Its use has not been attended by jaundice or other signs of hepatotoxicity,[1,3] as encountered with chlorpromazine,[7,8] the chloro analogue of trifluprομazine.

Reports of the effective control of retching and vomiting with trifluprομazine,[5] regardless of the cause of these symptoms,[6] were impressive. Nausea and vomiting are common in hospital practice. In debilitated patients and particularly in patients such as those included in this study, who are receiving therapy with alkylating agents such as nitrogen mustard, these symptoms not only are distressing but often resist treatment. A number of drugs have been used in attempts to control these symptoms, with varying degrees of effectiveness but with limited usefulness. This study was therefore undertaken to evaluate the efficacy

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of trifluprom azine in patients with nausea and vomiting from various causes, particularly due to nitrogen mustard therapy.

Method

A group of 29 patients (12 men, 17 women) ranging in age from 24 to 81 years were given trifluprom azine. All had pernicious nausea and vomiting. Nine had hepatic disease, congestive heart failure, cerebral aneurysm or migraine, and the remaining 20 had malignant disease, in the majority of cases metastatic. Table 1 lists the immediate causes of vomiting.

All the patients had received chlorpromazine or dimenhydrinate, or both, in 50 mg. doses intramuscularly, in an attempt to control the vomiting. These drugs were administered successively, in the event of failure, or during subsequent episodes for the purpose of comparison.

Trifluprom azine was administered by continuous intravenous infusion over a five to eight hour period, as indicated, 4 mg. being introduced directly into the intravenous tubing as a single rapid dose and 10 mg. being added to the intravenous solution (500 cc. of 5 per cent dextrose or normal saline solution, or, in some cases, blood). A waiting period of 15 minutes was allowed before trifluprom azine was given to the patients receiving nitrogen mustard therapy; by that time the nitrogen mustard had become fixed in the reticuloendothelial system and could not be altered by other administered drugs. Three patients with migraine received only a single 4 mg. intravenous dose of trifluprom azine.

Results

Table 2 shows the response of patients to antiemetic therapy with trifluprom azine compared with chlorpromazine and dimenhydrinate. Every patient obtained some degree of relief of nausea and vomiting after receiving trifluprom azine. The response was considered excellent or good in 27 of the 29 cases, i.e., the nausea and vomiting were promptly and completely relieved for a considerable period, usually six to eight hours. In most instances one course of therapy was sufficient to arrest the vomiting. A number of the patients were able to tolerate oral feedings without recurrence of vomiting. In two cases the clinical response to trifluprom azine was considered only fair, i.e., the vomiting subsided but nausea recurred intermittently. In all cases but one, trifluprom azine was superior to chlorpromazine or dimenhydrinate as an antiemetic agent. This evaluation was based not only on the control of vomiting but also on the patient's subsequent course. One patient with cerebral metastases who had nausea of vestibular origin responded better to treatment with dimenhydrinate.

TABLE 1

TRIFLUPROMAZINE AS AN ANTIEMETIC AGENT; IMMEDIATE CAUSES OF VOMITING IN 29 PATIENTS

Nitrogen mustard therapy	12
Jaundice	3
Cerebellar metastases	3
Aneurysm of anterior cerebral artery	1
Postoperative vomiting	1
Radiation sickness	3
Drug toxicity	5
Migraine	3
Severe gastritis	1

Side effects were not a problem with trifluprom azine. Sixteen patients had a transitory drop in blood pressure of 10 to 20 mm. Hg systolic, but in no instance was this hypotensive effect detrimental or supportive medication required. Drowsiness was noted in every patient, but this was not an undesirable effect since the majority of the patients were emotionally upset because of their distressing symptoms. Jaundice did not develop in any case. The patients in whom jaundice was present at the time of treatment with trifluprom azine continued to improve clinically during treatment, as demonstrated by liver function studies. Dermatitis was not encountered in any case. One patient in whom a severe skin rash developed after an injection of chlorpromazine was subsequently treated with trifluprom azine and the rash subsided.

The mechanism of the antiemetic action of trifluprom azine is not known, but the drug may act on the vomiting trigger zone in the medulla.

TABLE 2

ANTIEMETIC RESPONSE TO TRIFLUPROMAZINE COMPARED WITH CHLORPROMAZINE AND DIMENHYDRINATE

PATIENT, AGE AND SEX	DIAGNOSIS	ETIOLOGY OF VOMITING	RESULTS			REMARKS
			Chlorpromazine	*Dimenhydrinate*	*Trifluprom azine*	
J. A. 36 F	Carcinoma of breast, pleural metastases	Intrapleural nitrogen mustard	Good	Poor	Excellent	After triflupromazine, patient tolerated oral feedings without emesis
S. B. 42 F	Carcinoma of breast	Postanesthesia	None	None	Good	Vomiting did not recur after triflupromazine therapy
F. M. 44 F	Carcinoma of breast, bilateral pleural involvement	Nitrogen mustard	Excellent	None	Excellent	Emesis completely controlled by triflupromazine
M. K. 48 F	Carcinoma of breast, cerebellar metastases	Cerebellar metastases	None	Fair	Excellent	Patient received oral feedings after three days' treatment with triflupromazine
J. S. 48 F	Generalized metastases, carcinoma of breast	Anxiety state, anorexia, radiation	Fair	None	Excellent	Patient received oral feedings 24 hours after triflupromazine
A. T. 49 F	Generalized carcinomatosis	Nitrogen mustard	Excellent	None	Excellent	Patient was eating on third day after treatment with triflupromazine was begun
G. J. 50 F	Carcinoma of breast, hepatic metastases	Jaundice, nitrogen mustard in peritoneum	(Not used)	None	Excellent	Course of nitrogen mustard completed control of vomiting maintained with triflupromazine
M. R. 50 F	Metastatic carcinoma of breast	Drug toxicity	Severe skin rash	None	Excellent	Rash which followed intramuscular chlorpromazine, 50 mg., did not become worse after triflupromazine was adminis tered, and subsided in three days
F. T. 52 F	Generalized carcinomatosis, primary carcinoma of breast	Jaundice, nitrogen mustard	(Not used)	None	Excellent	Patient received oral feedings after four days' therapy with triflupromazine
B. G. 55 F	Migraine and islet cell tumor	Migraine	Excellent	Excellent	Excellent	Patient received 4 mg. triflupromazine intravenously
L. M. 57 F	Migraine	Ergotamine	Fair	Fair	Excellent	Triflupromazine abolished emesis
J. K. 58 F	Cholangiolitic jaundice	Drug toxicity	(Not used)	Fair	Excellent	After triflupromazine, vomiting subsided and jaundice was not aggravated
T. D. 58 F	Carcinoma of breast, cerebellar metastases	Cerebellar metastases, hypokalemia	None	None	Good	Vomiting did not recur after triflupromazine therapy

TABLE 2 *(Continued)*

ANTIEMETIC RESPONSE TO TRIFLUPROMAZINE COMPARED WITH CHLORPROMAZINE AND DIMENHYDRINATE

PATIENT, AGE AND SEX	DIAGNOSIS	ETIOLOGY OF VOMITING	RESULTS			REMARKS
			Chlorpromazine	*Dimenhydrinate*	*Triflupromazine*	
L. S. 62 F	Carcinoma of breast, pleural metastases	Nitrogen mustard	Good	None	Excellent	Vomiting did not recur after triflupromazine therapy
M. C. 69 F	Carcinoma of breast, cerebellar metastases	Cerebellar metastases, vestibular	Fair	Excellent	Fair	Dimenhydrinate gave better results than triflupromazine
C. W. 76 F	Carcinoma of breast, pleural and cerebellar metastases	Nitrogen mustard, adrenal insufficiency	Stupor	Fair	Good	Patient able to accept oral feedings after correction of adrenal insufficiency
N. A. 24 M	Migraine	Ergotamine	(Not used)	Fair	Excellent	Triflupromazine, 4 mg. intravenously, abolished nausea and vomiting
H. G. 35 M	Cholangiolitic jaundice	Drug toxicity	(Not used)	Fair	Excellent	Vomiting subsided and jaundice was not aggravated by triflupromazine
W. M. 44 M	Lymphosarcoma	Nitrogen mustard	Fair	Fair	Fair	Required continuous drip therapy with triflupromazine for partial relief of vomiting
M. W. 51 M	Metastatic carcinoma of pancreas	Severe jaundice	(Not used)	Fair	Excellent	Patient tolerated oral feedings after treatment with triflupromazine
W. H. 56 M	Hodgkin's disease	Nitrogen mustard	Fair	Fair	Excellent	Course of nitrogen mustard completed without recurrent vomiting
J. B. 62 M	Status epilepticus	Drug toxicity, pneumoencephalography	(Not used)	None	Excellent	No recurrence of vomiting 24 hours after triflupromazine
S. R. 62 M	Cholecystitis	Gastritis	(Not used)	Fair	Excellent	Patient free of vomiting after triflupromazine therapy
J. V. 68 M	Metastatic carcinoma, mandible	Nitrogen mustard, actinomycin C, radiation	Excellent	Poor	Excellent	Patient able to complete nitrogen mustard therapy without vomiting
H. H. 81 M	Congestive heart-failure	Digitalis toxicity	(Not used)	None	Excellent	Immediate cessation of vomiting achieved with triflupromazine
M. B. 47 M	Cerebral aneurysm	Marked vertigo	Fair	Fair	Excellent	Patient remained free of vomiting. Carotid artery ligation
W. M. 45 M	Lymphosarcoma	Nitrogen mustard	Good	(Not used)	Excellent	Triflupromazine gave immediate relief of vomiting
J. E. 45 M	Hodgkin's disease	Nitrogen mustard	Excellent	(Not used)	Excellent	Patient tolerated oral feedings after administration of triflupromazine
L. J. 52 F	Metastatic carcinoma, breast	X-ray radiation	(Not used)	Fair	Excellent	Immediate and continued relief of symptoms obtained with triflupromazine

Summary

Twenty-nine patients with active nausea and vomiting were successfully treated with trifluprομazine. In 15 patients, drug toxicity was the cause of vomiting, nitrogen mustard being the principal causative agent. In the remaining cases the vomiting was postoperative or was associated with jaundice, cerebellar metastases, migraine, radiation sickness, gastritis or cerebral aneurysm. All the patients had received chlorpromazine or dimenhydrinate previously. Trifluprομazine proved to be superior to these other drugs in every case except one, in which dimenhydrinate afforded better control of vomiting.

On the basis of the observations made during this study, it appears that trifluprομazine is a highly effective agent in the elimination and the prevention of nausea and vomiting of varied causes.

ADDENDUM

Four cases of persistent hiccup also have been treated with a single intravenous injection of 4 mg. of trifluprομazine. Relief was prompt and permanent. Trifluprομazine seems to be an effective agent in arresting persistent hiccup.

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Duquesne "Tamburitzans" to Perform at Interstate Assembly

The second evening of the 1960 Interstate Assembly will feature a novel program of folk songs and dances by the widely known Tamburitzans of Duquesne University in Pittsburgh. Part of the program cost is being assumed by the Assembly so that the ticket charge will be only $1.00. Tickets may be secured with advance registration or purchased at the Assembly.

For complete Assembly program and advance registration, write to Erwin R. Schmidt, M.D., Box 1109, Madison 1, Wisconsin.

The 1960 Interstate Assembly will be held at the Pittsburgh-Hilton Hotel, October 31-November 3.

SCIENTIFIC EXHIBIT

Meconium Ileus

A Medical and Surgical Challenge

Fibrocystic Disease of the Pancreas

↓

Diminished Intestinal Enzymes

↓

Abnormal, Obstructing Meconium

↓

Neonatal Surgical Emergency

HARRY C. BISHOP, JOHN W. HOPE
AND C. EVERETT KOOP

University of Pennsylvania School of Medicine and
Children's Hospital of Philadelphia, Philadelphia

Adapted from an exhibit at the annual meeting of the American College of Surgeons, Atlantic City.

Clinical and Roentgenographic Diagnosis

Clinical Indications

Progressive abdominal distention from birth

Bile-stained vomiting

Absent or abnormal, scanty stools

Dilated loops and visible peristalsis beneath thin, shiny abdominal wall

"Putty" sign—firm intestinal loops retaining an indented shape

Possible family history of fibrocystic disease

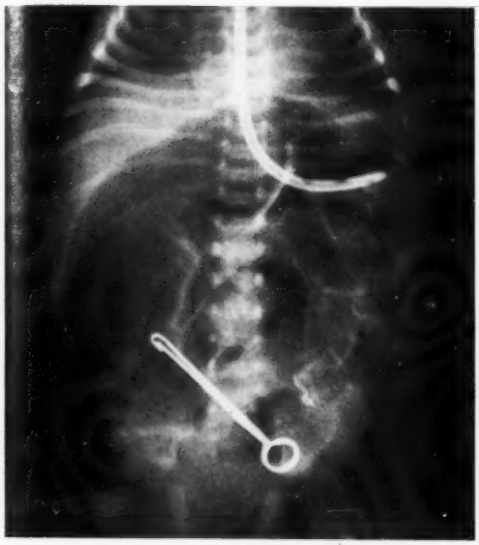
Supine

Small bowel loops of varying sizes and classic density of abnormal meconium in intestinal obstruction. "Soap bubbles" are seen within the meconium.

Erect

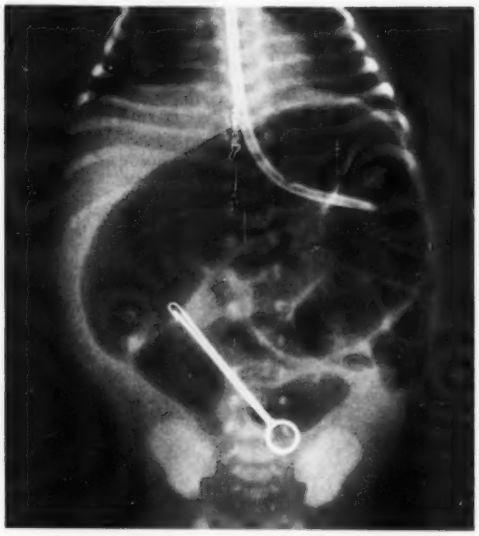
Intestinal obstruction with absence of fluid levels. Meconium shadows are in the same positions.

Supine

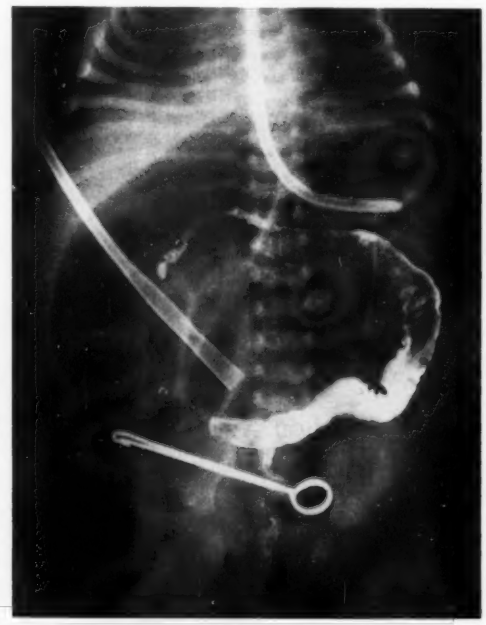


Varying sizes of small bowel loops in intestinal obstruction suggestive of meconium ileus. No "soap bubbles" are seen.

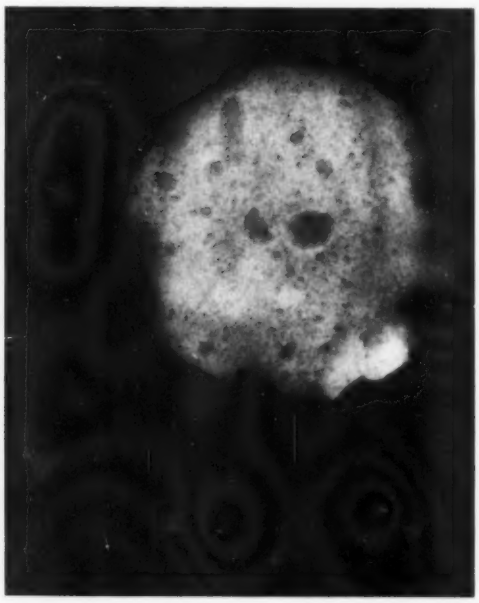
Erect



Absence of fluid levels in intestinal obstruction. It is impossible to determine whether distention of the large bowel also is present.

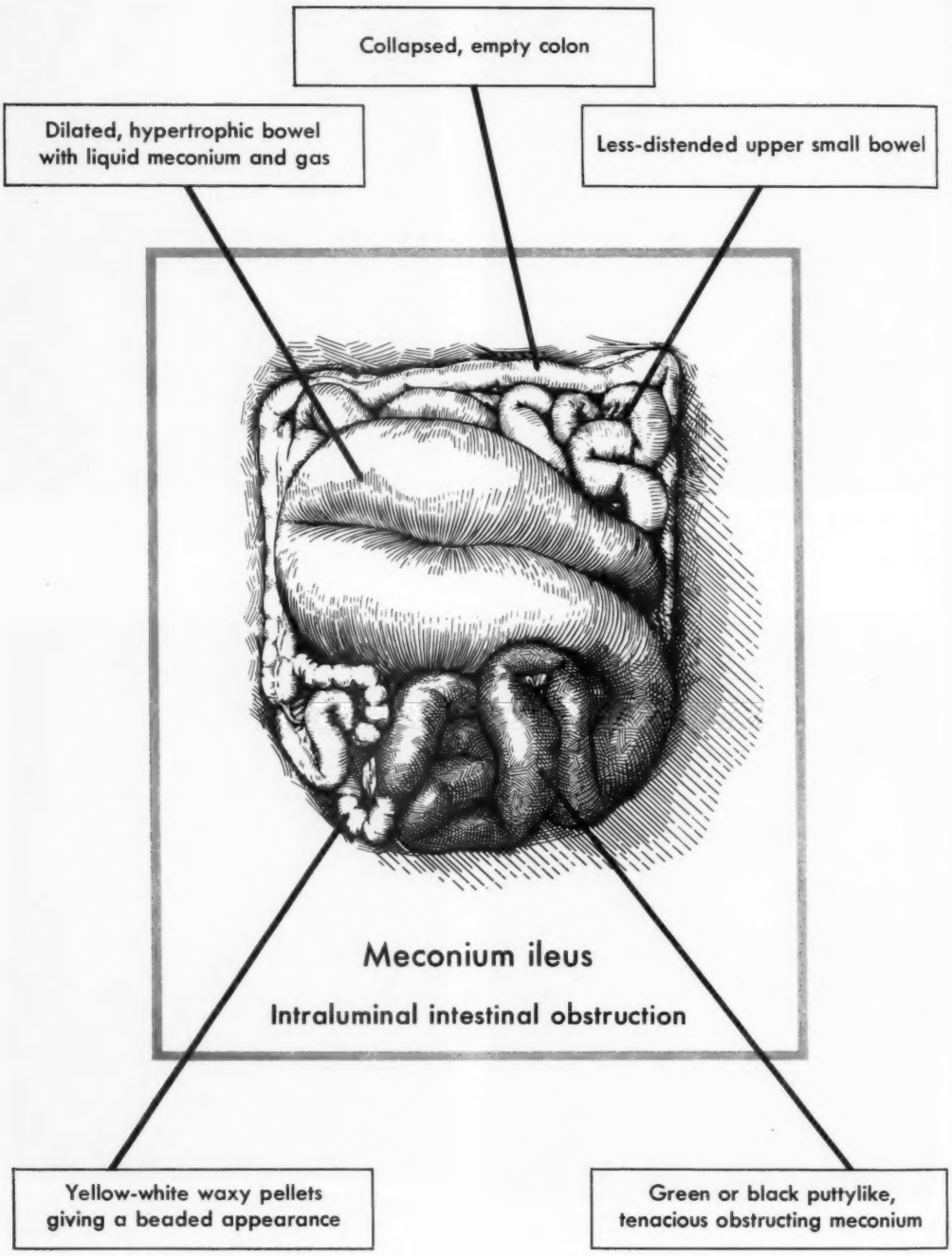


Barium enema showing normal, small and as yet unused colon.

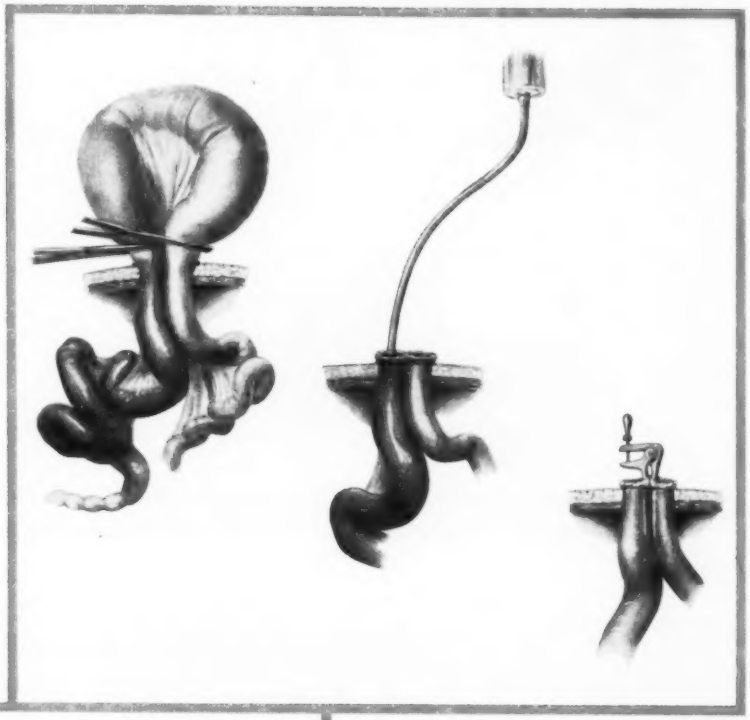


Abnormal, viscid meconium with small radiolucent areas ("soap bubbles") caused by air. The large radiolucent areas are due to injected air in vitro.

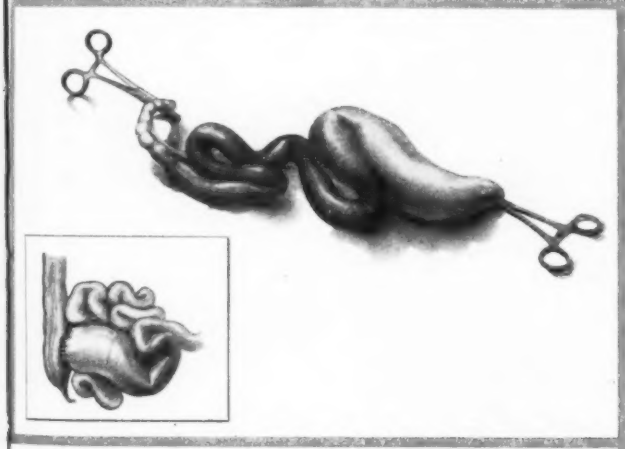
Pathology


Collapsed, empty colon
Dilated, hypertrophic bowel with liquid meconium and gas
Less-distended upper small bowel
Meconium ileus
Intraluminal intestinal obstruction
Yellow-white waxy pellets giving a beaded appearance
Green or black puttylike, tenacious obstructing meconium

Methods of Surgical Management



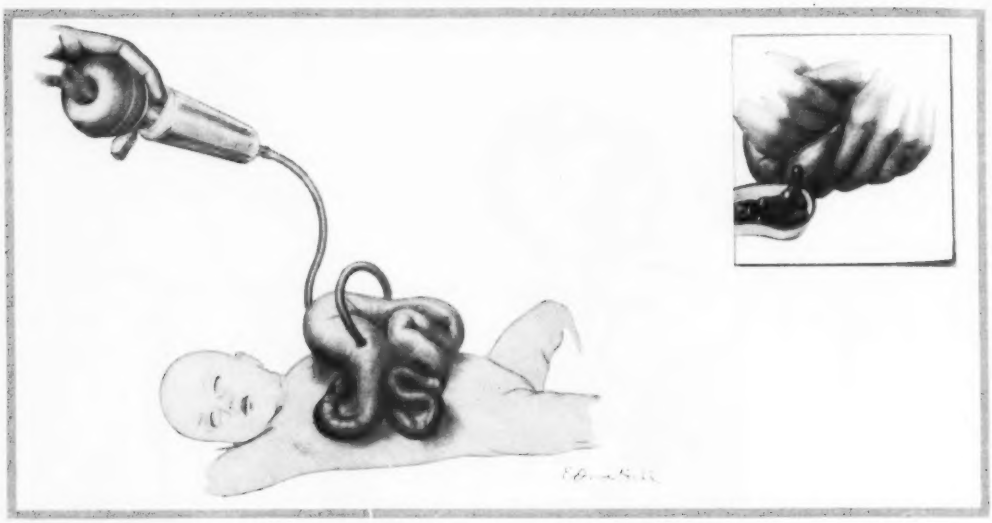
An aseptic Mikulicz resection and ileostomy, followed by irrigation with enzymes and secondary extraperitoneal closure.



Massive resection and primary anastomosis.

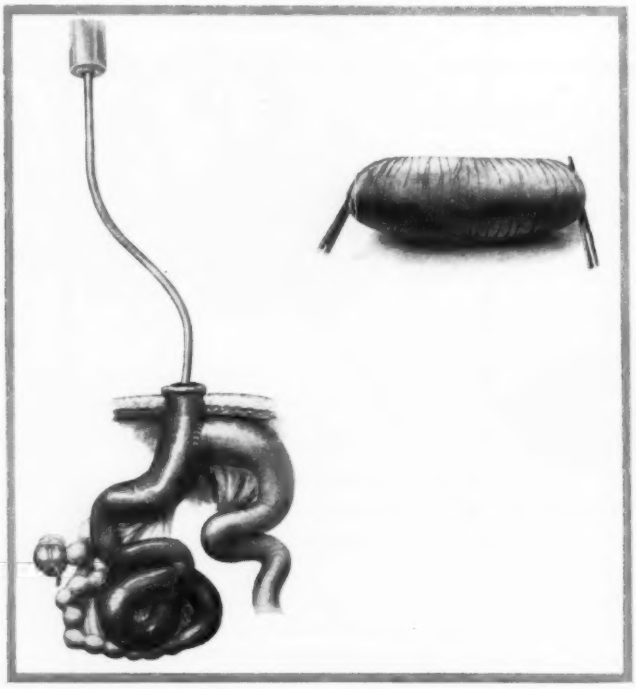
Loop ileostomy followed by irrigation with enzymes and by secondary intraperitoneal closure.

Methods of Surgical Management



Ileostomy followed by irrigation with saline or hydrogen peroxide and manual evacuation of meconium.

Our Choice of Surgical Procedure



Resection with a Roux "en Y" anastomosis and ileostomy, followed by irrigation with pancreatic enzymes and secondary extraperitoneal closure.

Later Medical Problems

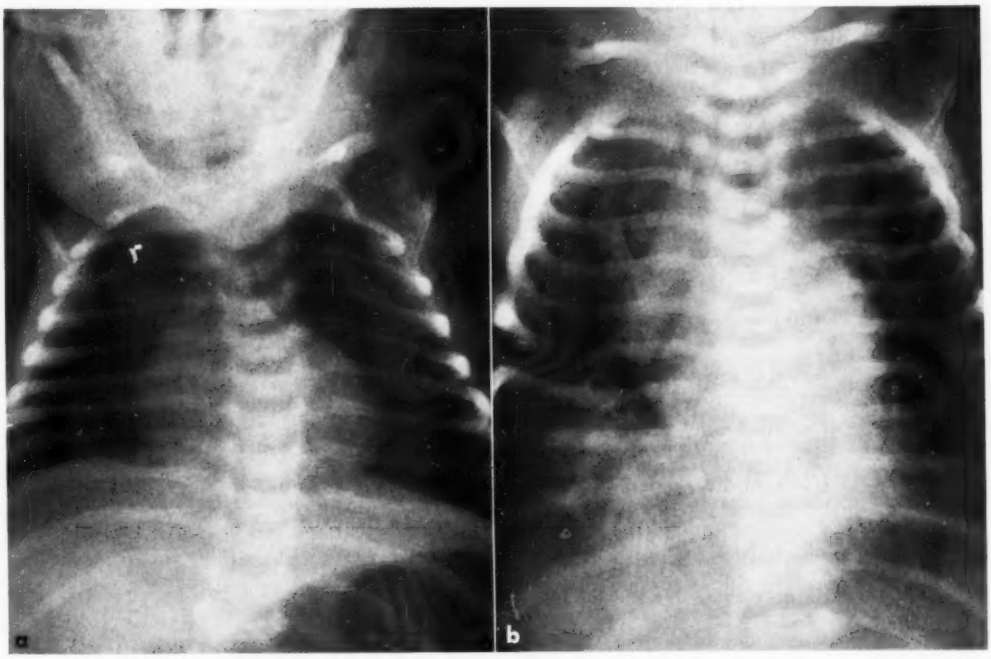
Fibrocystic Disease of the Pancreas Is a Generalized Disease of Exocrine Glands

Glands Involved

Pancreatic acini	Intestinal mucous glands
Bronchial glands	Salivary glands
Sweat glands	Biliary tract epithelium

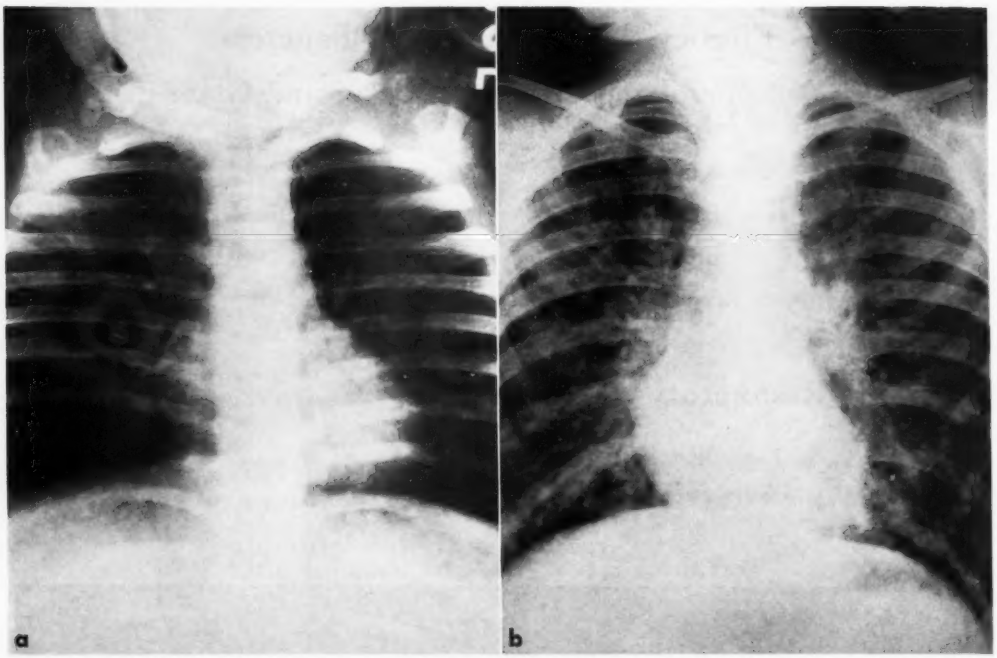
The Respiratory Tract Problem; Often a Late Cause of Death

Viscid Mucus → Atelectasis / Obstructive Emphysema → Chronic Infection → Pulmonary Insufficiency



Rapid pulmonary involvement following relief of meconium ileus in an infant at two days (a) and 28 days (b) of age. The infant died at 30 days of age.

Later Medical Problems



Progressive pulmonary involvement in a child at one year (a) and four years (b) of age. The child died at age four.

Medical Management

Add pancreatic extracts to diet

Avoid exposure to respiratory infections

Use antibiotics judiciously (prolonged, rotating administration)

Use humidity, expectorants, bronchodilators and postural drainage

Increase vitamin intake

Replace excessive sodium chloride losses from sweating

Search for unsuspected disease in siblings

Food Faddism—A Growing Threat

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THE history of food faddism is fascinating, and it would be entertaining, if it were not repeating and extending itself today. Throughout the records of man's efforts to lessen pain, cure disease, and forestall or perhaps prevent death, the charlatans and quacks have received top billing. Despite our remarkable advance in knowledge, nonsense has never interfered more effectively with the application of the science of nutrition in the feeding of Americans, sick and well. Human beings are obviously incurably credulous! At the present time, the prognosis is not good.

The extent of the problem and the cost to the consumer are amply documented in the records of the Food and Drug Administration, the American Medical Association, the Better Business Bureau, the United States Post Office, and the Federal Trade Commission. It is a strange paradox that the decades which have seen a rapid advancement in the science of nutrition have also seen this fantastic increase in products, pills and panaceas offered through misleading advertising and expounded by irresponsible nutrition "lecturers" and "writers."

Factors Influencing Food Faddism

Many factors have influenced and in some way contributed to this unhappy situation, but a few examples may be cited of the details of the environmental mosaic against which faddism continues to thrive.

Our means of communication have become so effective that the limited influence of yesterday's medicine man has expanded into a barrage of misinformation through the channels of radio, television, newspapers, magazines, itinerant health lecturers and persistent door-to-door salesmen.

Testifying before a congressional committee on false and misleading advertising, Dr. S. William Kalb[1] stressed the significance of

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modern communication media in the rapid spread of misinformation:

> The old-time medicine man, yesterday's nutrition quack, sold his cure-all, youth-restoring patent medicines to the small groups he was able to attract to a show on a street corner, in a vacant lot, or at picnics and fairs. He operated in a very small way under conditions of relatively limited communication and slow spread of public information. Improvements in communication make possible the rapid and widespread dissemination of information. An informed public became conscious of the lack of effectiveness of cure-alls in the patent medicines. Exposed, deprived of his protecting cloud of mystery and ignorance, the medicine man disappeared from the scenes some 20 years ago; or did he?
>
> Too good to be true, this disappearing act was in itself an illusion. Adapting himself to a changing time and conditions, to a better-informed public, the medicine man became a food expert or a drug expert dealing in so-called health foods and drugs and diet supplements instead of patent medicines. Ironically, it is the food faddist who has recognized and made use of the opportunity afforded by our modern communication methods to reach and influence great numbers of people quickly and effectively.

In the "good old days," it took months for a manufacturer of patent medicines to inform only a few thousand citizens about his newest remedy. Today, a manufacturer can enlighten millions of potential customers about equally ineffective products in the seconds allotted to a commercial on the airwaves.

The mysteries and magic of food make good copy because scientists are the first to acknowledge their limited but rapidly growing understanding of the specific role of certain nutrients in human nutrition. Furthermore, theories and postulates, evolved by investigators and reported for the information of their professional colleagues, are often quoted as proved and accepted facts by promoters who find an isolated statement useful in their misleading but often convincing advertising copy. Because a scientific report may become the faddist's sales instrument, investigators find it necessary to control their enthusiasm when reporting results with products they use in clinical trials.

In each scientific announcement of evidence demonstrating a need for or the usefulness of a particular nutrient for the well-being of a mouse or a monkey, the faddists recognize fertile soil for another story, another product and additional profit. Through ignorance, indifference or plain dishonesty, faddists fail to realize the hazards of transferring isolated findings from experiments with animals to widespread application in human nutrition. Royal jelly may be beneficial to the queen bee, but it is certainly no panacea in the human race. Surely, scientists will not step from behind the barriers raised by conservatism, honesty and ethics to make false claims and unrealistic promises. The faddists capitalize on the very characteristics that are the pride of professional persons.

Our economy has permitted people to spend money for expensive dietary supplements, health foods, health lectures and "miracle" cooking utensils. Perhaps some faddists would spend their last dime for such luxuries, but it is likely that faddism would not be as expensive if the economy could not bear it. Copywriters do an excellent job of aiming much of their "come-on" about "new, unknown to medical science" hokum toward older citizens whose income may be too limited to permit both supplements and good food.

Newspaper advertising for "Lipitrons," for example, opened with the words:[2]

> If you are over 35 years old. . . . If you are getting that "growing old" feeling. . . . Science has now found how to fight that feeling of "growing old." . . .
>
> LIPITRONS
>
> *For you* if you feel tired and weak and run-down!
>
> *For you* to help you recapture lost vitality and strength!
>
> *For you* to combat nervousness, lack of vigor and energy!

The complete advertising copy created the impression that the drug was effective in the treatment of persons over 35 years old to combat that feeling of growing old; to relieve tiredness, weakness, nervousness and a run-down condition; to overcome the deficiencies

that help drag one down; for premature advancing age; to furnish a whole new world of buoyant energy, vitality and strength by relieving and overcoming the basic causes of their nutritional deficiencies; to help those who feel years older than their age to enjoy life again; to regain vigor and vibrant energy; to enable thousands of men and women to work harder, etc., *ad nauseam*. The United States District Court of Nebraska found the corporation and the defendant guilty on all counts.

The court decision in this case includes a statement of the concern which we have today as advertising copy continues to bombard older people with vague promises and empty guarantees for rejuvenation at a price.

> The present drugs and their supporting publicity would have no appeal and little meaning to young persons, athletes, high school or university students, youthful workers, or business or professional people. But it is quite otherwise with men and women beyond middle age, the so-called older folk of the type pictured in the challenged newspaper advertising. As most members of the federal judiciary will at once realize, those oldsters need little more than a vagrant suggestion to lead them to hope in the restorative ministry claimed for the defendants' tablets. Their publicity advances a message they are longing to read or hear; and with pathetic eagerness they receive and embrace it. They must especially be regarded in these circumstances, for it is to them and their faltering faculties, physical and mental, that the message of the labeling is oriented. Thus understood, the court has no difficulty in concluding that the labels and labeling are false and misleading. What, indeed, can be more cruelly false and misleading than the inspiration of hope in one for whom actually there is no hope?[3]

The book "Arthritis and Common Sense"[4] has had such wide appeal in its own misleading way that the Council on Foods and Nutrition of the American Medical Association devoted an editorial to the topic, "Who treats arthritis?"[5] and urged physicians to peruse this book. The Council declared: "There are those individuals who do not ask their physician's advice. They may very possibly be in the majority, indicating an even more important reason for the physician to be aware of this type of literature. Is it not one of his responsibilities to his community and to his profession to exert all of the influence he can in combating food and health misinformation whenever and wherever it may occur?"

The fact that "Folk Medicine. A Vermont Doctor's Guide to Good Health"[6] was written by a member of the American Medical Association (licensed to practice medicine in 1904) has provided it with much prestige. The sales figures for this book give evidence of a desire of thousands of our citizens to consider and perhaps accept the author's new theory (honey and apple cider vinegar) on the treatment and prevention of diseases ranging from the common cold to arthritis and "many others which often defy conventional medical diagnosis and treatment." The aged country doctor has added to the confused state of affairs in the field of weight reduction by suggesting that "the apple cider vinegar will have made it possible to burn the fat in the body instead of storing it . . . ."

Some people obviously enjoy being "on a diet" and championing a "cause." They are certain to become the center of conversation when they launch out to defend their latest dietary excursion. It is likely that this need will always be apparent in a segment of the population, and it is also likely that faddists may harm themselves much less if they lose themselves in the wonders of blackstrap molasses, kelp, volcanic ash, crude salt, alfalfa, water cress, parsley and garlic than if they develop an equally fanatic program involving other kinds of misguided health practices. The specific foods are not likely to harm the customer, but delay in seeking medical attention for the vague symptoms faddists love to describe may be costly.

Human beings appear to gravitate toward the simplest explanation of a phenomenon. It may be a dishonest answer but it *is* simple! The faddists are alert to the concerns of the nondiscriminating public and capitalize on fears or, if necessary, create fear.

The medical profession honestly admits that a simple, direct and "guaranteed or your

money back" cure has not yet been recognized for cancer, diabetes, arthritis, multiple sclerosis and many other diseases. One would hope that when medical knowledge has advanced considerably in a special field, the public would be grateful and would be wary of nonmedical treatment. This has not been true in the case of diabetes.

Within recent years, the Food and Drug Administration has taken action against two products, because claims that these drugs were effective against diabetes could not be substantiated. The Kaadt Diabetic Institute distributed "a drug or treatment consisting principally of a mixture of vinegar and potassium nitrate (saltpeter); TAKA-DIASTASE®, a proprietary digestive preparation, was sometimes added, but analysis revealed no Taka-Diastase because it is inactivated and destroyed in a solution as strongly acid as the vinegar medicine."[7] Diabena also proved useless to diabetics.[8] In part, the label on this drug read: "Kiabena-alcohol 12½%. Active ingredients: tephrosiavirginiana, lithii citras, cinnamon, food coloring. Dose: Two teaspoonfuls every four hours in water. Children in proportion to age."

At the present writing, it appears that as long as there are diabetic customers, there will be diabetic "cures." Furthermore, as long as there are diseases for which no effective cure is known, the faddists will bridge the gap between the patient's concern and his pocketbook with miracle products and extravagant promises.

Label information and advertising copy for a single product may be so completely different that it is sometimes difficult to realize that both could possibly relate to one and the same product. While the label declarations are under the jurisdiction of the Food and Drug Administration, advertising claims are under regulations of the Federal Trade Commission.

People are motivated to buy a product through the advertising they see or hear. Few consumers will carry an ad with them to the store and try to compare the promises in print with the facts presented on the label. The Food and Drug Administration's influence has been evidenced in the area of labeling, but the Federal Trade Commission's regulations have not been much of a handicap to those who wish to write advertising copy in misleading ways. Furthermore, the purveyor of misinformation has time in his favor. The question of the length of time involved in the removal of objectionable products from the market and of misleading advertising from the various communication media was one of the problems discussed at the Blatnick Committee hearings.[9]

It is not within the purpose of this paper to discuss the development of the laws now operating to protect the public from misinformation and fraudulence in the field of nutrition. It is suggested, however, that members of the medical profession, collectively and individually, attempt to determine ways in which more money, personnel, research facilities and effective legislation can be obtained so that the faddists will find misleading the public less lucrative and, hence, less alluring than it is now.

According to Paul L. Day,[10] Scientific Director of the Food and Drug Administration, "The Federal Government spends less than seven cents per person each year for protection of foods, drugs and cosmetics against adulteration, misbranding, filth and decomposition; protection against dangerous drugs and cosmetics and the hazards of pesticide residues and radioactivity; and all the other enforcement and research activities of the Food and Drug Administration . . . . Expressed in another way, Congress appropriates to the Food and Drug Administration each year less than one-sixth of the cost of one military jet bomber."

Accomplishments by our federal agencies with existing shortages of money and personnel have been noteworthy. The job they face is just too big; no matter how dedicated the inspectors, sincere the scientists, or eager the administrators, dedication and enthusiasm without adequate staff and funds cannot result in the removal of these serious threats to medical care in the United States.

Our programs in nutrition education for children and adults have fallen far short of helping them to make decisions based on facts

rather than on the emotional and irresponsible appeal of the faddists and charlatans. Education should prove the most effective weapon in limiting the faddists' influence.

Why Be Concerned?

Doorstep diagnosis and mail-order treatment are foolish and vicious. When confidence is placed in nonmedical diagnosis and money is invested in products ranging from pumpkin seeds to Pacific Ocean water, the least the customer will lose is his money, the most—his life. In any event, the customer will be assured that the medical profession has nothing quite like it to offer—thank goodness!

Many of the dietary supplements are suggested to cure (or the distributor assumes the freedom to so imply) as many or more diseases as there are ingredients on the label. "Shotgun" therapy is not new. Andromachus, physician to Nero, once provided his royal patient with a remedy containing 78 ingredients, an affair only a little more complex and uncertain than many dietary supplements being sold today. History reveals that Andromachus did not give large enough quantities of this toxic mess to kill the patient.

In Nero's day, when all products listed in the pharmacopeia were compounded into one medication, the term "theriaca" was used.[11] Today, we call such preparations dietary supplements. Although Nutrilite, Visan and Vit-Ra Tox include somewhat fewer than 78 ingredients, in the field of nutrition they might be considered present-day theriacas.

The cost of membership in health organizations; the cost of lecture series, pills and health foods; and the support of health ranches are great. Many of the products are sold on a "plan" basis. Vitasafe and Nutrilite customers, for example, are thus *assured* of regular delivery and the manufacturer is confident of a steady income! Yet, occasionally, one hears the plaintive cry that "medical care is too costly; I can't afford it." Cook[12] reported that in 1957 more than $1 billion was spent for patent medicines and that the Nutrilite Company alone had more than 20,000 "distributors" who sold tens of millions of dollars worth of dietary supplements.

In an initial decision[13] by a Federal Trade Commission examiner, dated January 11, 1960, the statement was made that Mytinger and Casselberry, Inc. have contracts with more than 80,000 house-to-house distributors of its Nutrilite Food Supplement.

The Fuller Brush Company has seen fit to add a line of vitamin and mineral supplements. Mail-order vitamins have huge sales volumes, to say nothing of such sales by supermarkets and health food stores. "Lecturers" draw large crowds, particularly after they have been "persecuted" and sent off for jail sentences, and they do not share their "fabulous" discoveries without adequate reimbursement. If all the money spent for empty dreams in the name of food faddism could be directed toward research and education, the solution of some of the unanswered questions in nutrition and in medicine might be forthcoming more rapidly.

Finally, choice of food is apt to be erratic. It is likely that if more money is spent on health foods and specific nutrients, it will decrease the contribution of a sensibly planned diet of good American foods. Appreciation of the role of adequate food in health and in sickness will be delayed among thousands of our citizens until the faddists' influence is curtailed and our program of positive education is enlarged.

What Can Be Done?

To recognize the problem of food faddism for what it is and to recall some of the reasons why it exists are of purely academic interest if we make no concerted effort to combat it. "Organized medicine has led the fight against quackery, unethical practices and the misleading promotions of nostrum makers ever since the first meeting of the American Medical Association in Philadelphia in 1847. There, a resolution was introduced calling for renewed vigor in the fight against quackery and its attendant evils."[14]

For more than 50 years, the Bureau of Investigation of the American Medical Association has been a clearing house for information regarding quacks and their methods of operation. For more than 40 years, members of the

American Dietetic Association have attempted to combat fraud with fact. The Food and Drug Administration has worked diligently; the Food, Drug and Cosmetic Act of 1938 was a milestone in the fight against quackery. The Better Business Bureau and the United States Post Office have contributed in a forthright manner. It is obvious, however, that a more vigorous program of education is needed, and the American Medical Association, in cooperation with the Food and Drug Administration and the Better Business Bureau, has taken bold steps to provide every interested physician with the information and the tools he needs to assume leadership in a nationwide program to combat ignorance with education in nutrition.

The following aids are available for your use in planning a program in your community:

1. A materials kit entitled "Food Faddism and False Claims" is available from the American Medical Association. This kit includes reprints, a 20 minute speech, a bibliography and descriptions of a film and an exhibit recently prepared by the Association.

2. The film entitled "The Medicine Man" is cleared for television use and will also prove helpful in your community program. A small flyer entitled "The merchants of menace" is planned to be distributed to the film audience, and reprints of "Let 'em eat hay," from the September 1958 issue of *Today's Health*, will provide excellent follow-up reading for those who have been motivated by the film to appreciate the problem of faddism. The film runs 27 minutes and can serve as an excellent introduction to a lively discussion. The use of this film as part of the community service program of a local medical association is highly recommended.

3. The exhibit on "Nutrition Nonsense and False Claims" is so attention-getting that you will find it necessary to plan for a long-time display. This is also available on loan from the American Medical Association.

4. The January 3, 1959 issue of the *Journal of the American Medical Association* carried a statement on "Vitamin preparations as dietary supplements and as therapeutic agents."[15] This summarized the recommendations of the Council on Foods and Nutrition relative to kinds and amounts of vitamin and mineral supplements considered useful under various conditions of stress.

5. The Council on Foods and Nutrition of the American Medical Association also has published a compilation of statements and decisions.[16] This publication describes recommended advertising and terminology for labels and also spells out practices not acceptable in the advertising of food and dietary supplements. Unfortunately, you will find it very easy to assemble examples of the kind of advertising copy which the Council on Foods and Nutrition decries.

6. Your encouragement of greater circulation of the publication *Today's Health* is suggested, because the information on nutrition given in it is accurately and attractively presented. In 1958, this publication carried a series of 12 papers on nutrition. Reprints of these papers are available.

7. The American Dietetic Association[17] has published a pamphlet entitled "Food Facts Talk Back," a question and answer presentation. This useful publication is available from the American Dietetic Association, 620 North Michigan Avenue, Chicago 11.

8. The Nutrition Foundation, Inc.[18] has copies of a pamphlet entitled "The Role of Nutrition Education in Combating Food Fads" available for the asking. The role of the Food and Drug Administration and that of the Federal Trade Commission are described and a brief description of some of the faddists and their products is presented by members of the department of nutrition, Harvard School of Public Health.

9. In October 1959, the *New York Post* ran a series of six stories on "Foods, fads, facts and phonies." It is an excellent series and can be purchased in reprint form.

10. In order to appreciate fully that history is repeating itself, read "The Golden Age of Quackery."[19] It describes some of the multitude of cures available under the leaky umbrella of home remedies prior to 1907, when President Theodore Roosevelt's Pure Food and Drug Act altered the products and required honest labeling. While reading this

fascinating account of the so-called golden age of quackery, you may wonder how the present era of misleading advertising, nonmedical diagnosing, health store treatment, and nutrition lecturers with pots, pans, pamphlets and pills will be categorized. Will this be described as the diamond jubilee of food faddism? It is true that narcotics, alcohol, herbs and bark have been for the most part replaced by vitamins, minerals, seaweed, etc. The distributors have had to keep up to date! Ingredients have changed and the advertising copy has been altered with the years; yet, there is a strange likeness between the events described in "The Golden Age of Quackery" and those revealed by James Cook in "Remedies and Rackets."[12] The latter book will be most enjoyed after the former has set the stage. These books supplement each other and together they bring into sharp focus the problem with which the medical profession is faced today.

Summary

Nutritionists look to the medical profession for leadership in the renewed effort to lessen the influence of the quacks who are luring people away from sound dietary practices and ethical medical care. We want to support you in these efforts.

When professional groups consider food faddism unimportant, they are by their very indifference lending credence to the old adage that silence lends consent. Tools and information are available to us, but the implementation of an influential program will depend to a very great extent on the conviction and willingness of physicians to speak out loudly and effectively. Hopefully, a portion of the 10 million people who now live in the shadow of confusion can be motivated to seek ethical roads to good nutrition and medical care.

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CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Edited by William J. Gillesby, M.D., Assistant Chief, Surgical Service

Case Report

A 36 year old Negro man was admitted to Hines Veterans Administration Hospital on May 23, 1959, because of periumbilical griping pains of three months' duration. He said that at first the pain was temporarily relieved by milk, but not in recent weeks. The day before admission, he "strained himself" moving heavy furniture. That evening and the following morning he passed several dark, bloody stools. The abdominal pain ceased. The patient had not had nausea, vomiting or other gastrointestinal symptoms. He denied any heavy drinking immediately prior to the bleeding but admitted drinking whiskey and beer during the preceding week end, five days before admission. He frequently drank heavily on week ends but only occasionally drank during the week, when he took a shot of whiskey for his abdominal pain. The pain usually was worse on the day after week-end drinking.

The patient had never had previous gastrointestinal disease or been hospitalized. He had worked at different factory jobs, in the steel mills, and as a sand blaster, but had done only odd jobs for the past year. He smoked three-fourths of a package of cigarettes daily. He had gonorrhea at the age of 19 years. His parents and several siblings were all living and well.

Examination revealed a well-developed, well-nourished, muscular man appearing neither acutely nor chronically ill. He was alert, cooperative and pleasant. His height was 5 ft. 8 in. and he weighed 173 lb. His pulse rate was 88, and blood pressure 112/84. The nasal mucosa was inflamed and covered by a mucopurulent secretion. The tonsils were enlarged but not inflamed. There was a large soft-tissue mass approximately 10 cm. in diameter overlying the left scapula, which was considered to be a lipoma. The heart and lungs were normal. The abdomen was soft and not distended. Minimal tenderness was noted to the left of the umbilicus, but the right rectus muscle appeared to be more tense. No organs or masses were palpable. Bowel sounds were active. Rectal examination revealed red-tinged black feces.

The patient was treated initially with bed rest, gastric No. 1 diet, milk and antacid alternating every half hour, and phenobarbital. Blood pressure and pulse remained stable. He remained afebrile and asymptomatic. Stools returned to normal color two days after admission but were strongly positive for occult blood until June 5. After that date, two stools were negative for occult blood.

Urinalysis disclosed a specific gravity of 1.012, no sugar or protein, and negative findings microscopically. The initial hemoglobin

level was 11.5 gm. and the hematocrit was 38 per cent. On the second day the hemoglobin level was 13.9 gm. and the hematocrit 40 per cent; these values remained stable subsequently. The leukocyte count was 5200 with normal differential count. Sedimentation rate was 12 mm. and 20 mm. Serologic studies were negative. The nonprotein nitrogen level of the blood was 30 mg. four days after admission. Total protein measured 6.7 mg.; the albumin-globulin ratio was 4.3-2.4. The alkaline phosphatase content was 2.8 Bodansky units. The prothrombin time was 13 seconds (100 per cent).

A chest x-ray and an electrocardiogram were normal. On May 28, an esophogram and a gastrointestinal series revealed a "duodenal deformity." On June 5, esophagoscopic examination revealed an essentially normal esophagus with a few small veins in the lower portion about 1 mm. in diameter. Gastroscopic examination revealed persistent spasm in the pars media, and only the upper portion of the stomach could be visualized; this appeared normal. On June 8, a small bowel series disclosed "some dilation of a segment of terminal ileum with a suggested extrinsic pressure deformity of this portion of the ileum, raising the possibility of a mass." On June 9, a barium-enema study showed "dilation of terminal ileum with a suggestion of a tumor mass in the terminal ileum." On June 12, another small bowel series revealed multiple filling defects in the ileum. Laparotomy was performed on June 26.

Discussion

DR. ERWIN M. KAMMERLING (assistant professor of medicine, Chicago Medical School; attending physician, Cook County Hospital): We are concerned here with the case of a 36 year old Negro man who was admitted to the hospital on May 23, 1959, and underwent exploratory surgery approximately five weeks later, on June 26. His original story was of periumbilical griping pains temporarily relieved by milk. When a patient presents himself with periumbilical pains, even though they are relieved by milk, I would be concerned about faulty ducts someplace past the bulb, in the jejunum or ileum, and would make sure this area was investigated very carefully.

Shortly after the onset of the pain, he began to bleed and the pain disappeared. This, of course, is a quite common situation in gastroduodenal ulcer. A patient may have pain for days, weeks or months, and with the onset of bleeding often will have relief of pain for the first time. It is important that this patient did not have nausea, vomiting or other gastrointestinal symptoms. He had a vigorous alcoholic history, which he maintained consisted chiefly of week-end drinking with an occasional drink during the week—but ordinarily when a man takes a shot of whiskey for pain he is a pretty good drinker.

Physical examination was unrevealing. There is no mention of any fever, and the lipoma which was noted does not seem significant. In the abdomen there was limited tenderness to the left of the umbilicus, and the right rectus muscle appeared to be more tense; however, nothing more is said about that, and it is difficult to evaluate. Rectal examination revealed a red-tinged black stool.

He was treated conventionally for upper gastrointestinal bleeding and responded readily. He had no further pain, and stools became negative. Urinalysis revealed nothing abnormal, and he had a normal sedimentation rate. Then, five days after admission, x-rays were made, and an esophogram and an upper gastrointestinal series revealed a "duodenal deformity." Five days after bleeding, we can assume that vigorous palpation was not done, and under these circumstances if he had in addition to a "duodenal deformity" an ulcer niche it may not have been demonstrated. Esophagoscopic findings were essentially normal, as were gastroscopic findings. On June 8, about two weeks after admission, a small bowel series revealed "some dilation of a segment of terminal ileum with a suggested extrinsic pressure deformity of this portion of the ileum, raising the possibility of a mass."

DR. JAMES W. MIREE (physician in charge of x-ray therapy, radiology service): The esophagus, stomach and duodenum were normal. The duodenal loop was normal in appearance. A small bowel series on June 6 showed

FIGURE 1. Filling defect in terminal ileum.

FIGURE 2. Repeat gastrointestinal series, showing filling defect in terminal ileum.

a filling defect within the small bowel, in all probability in the ileum, with a little narrowing (figure 1). Another small bowel series was carried out a few days later, and still showed the filling defect, fairly round and smooth, in the terminal ileum (figures 2 and 3). There was a little intussusception and a smooth defect which moved around, and this makes one suspect the presence of a polypoid lesion of the *distal* ileum.

DR. KAMMERLING: The differential diagnosis, apart from the upper gastrointestinal tract, would concern primarily the lower bowel. The original description of the deformity, which mentions extrinsic pressure, raises the question of possible regional enteritis with an inflammatory mass of nodes pressing out and involving extrinsically an area of the small bowel, but it is not very likely that this is a case of regional enteritis with a mass in the distal bowel. Bleeding due to regional enteritis in an otherwise healthy Negro man certainly is not common. This man had not had difficulty prior to the onset of pain three months before hospitalization, he was afebrile at the time of admission, he did not appear very ill, and there were no previous signs to make one suspect regional enteritis. The incidence of regional enteritis in Negroes is not very great; I believe the first case actually was reported about 10 years ago.

The primary diagnosis in my mind obviously is a small bowel tumor, which often presents itself with bleeding or obstruction or anemia and weakness. Sometimes it will penetrate or perforate, but usually the findings are abdominal pain, anemia, obstructive symptoms or bleeding—bleeding, of course, being high on the list. Of the multiple tumors, one would first consider lymphosarcoma, lymphoma of the small bowel. In regard to the likelihood of ileotuberculosis in this area, the normal chest film and the fact that he was taken to the operating room without tuberculous medication speak against it. Could he have a benign tumor of the small bowel, an adenoma? Yes, he could have an adenoma, and he could have an adenocarcinoma of the small bowel. Whether he had a lymphoma or an adenoma or an adenocarcinoma I do not believe could be said.

What part did his alcoholic history play in

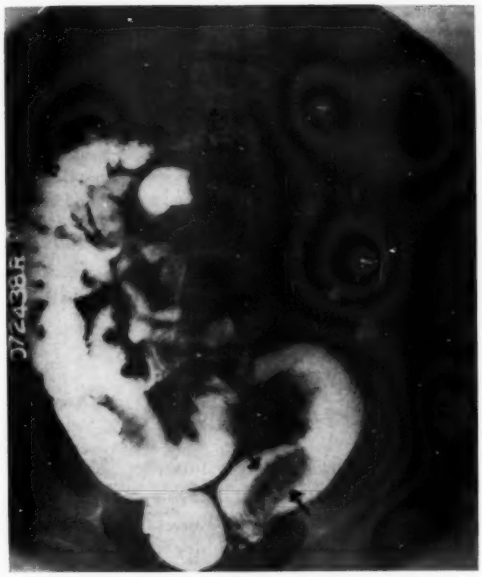

FIGURE 3. Another view of filling defect.

the upper gastrointestinal bleeding, in terms of alcoholic gastritis and duodenitis or of peptic ulcer exacerbated by bleeding? Could he have cirrhosis with bleeding from varices or ulcer? There is not much evidence for this. No mention is made of BROMSULPHALEIN® study, but, based on the paucity of other findings, the likelihood of liver disease with varices or bleeding ulcer is, I feel, very remote.

So I would say that he had a polypoid tumor of the distal small bowel, possibly a lymphoma, possibly adenoma or adenocarcinoma; and the surgeon or the pathologist would have to tell me further.

DR. ROBERT FRUIN (chief, gastroenterology section): The preoperative clinical diagnosis was small bowel tumor or possibly a large polyp.

DR. CALVIN RADIN (assistant chief, general medical section): Are the pictures that were shown incompatible completely with Meckel's diverticulum?

DR. KAMMERLING: That is a very fair question. I see nothing inconsistent in the possibility of abdominal pain with ulceration in a Meckel diverticulum, with penetration and an inflammatory mass in addition to the polypoid filling defect. In regard to the film itself, in terms of the well-circumscribed mass, I would be a little surprised if that is what it was; I have never seen one like this.

DR. ERVIN KAPLAN (acting associate director, radioisotope service): Dr. Kammerling spoke about the possibility of this being a carcinoma. I wish he would elaborate a little further on what type of carcinoma he might expect in the small bowel.

DR. KAMMERLING: Adenocarcinoma is the carcinoma I would expect. In one of the largest series I have seen reported, the incidence of benign lesions was approximately the same as that of malignant lesions in this area, and lymphoma and adenocarcinoma were the two malignant lesions.

DR. FRUIN: I might point out that the last case we had resembling this one, that of a patient who had three episodes of bleeding like this and had a somewhat similar x-ray, was a case of carcinoid.

DR. MYRON RUBNITZ (chief, laboratory service): From the rather extensive number of tumors that we see here, I cannot remember seeing an adenocarcinoma of the ileum. In the years I have been here, certainly lymphomas and carcinoids have headed the list of the malignant tumors that we have seen, by quite a good deal. In fact, we have not really seen many benign tumors, unless one included polyps, which also are rather unusual, really.

DR. ARNOLD LITTMAN (chief, medical service): Owing to the longitudinal disposition of this tumor, if it is a tumor, my first thought would certainly be of a benign intramural lesion, from the bulging out of the wall, such as a fibroma or a lipoma—some such category, rather than adenoma.

DR. KAMMERLING: Anyone who is bleeding briskly as high up as the stomach can have reddish-black stools—red-black, red and black stools. The fact that it is reddish would not make me suspect that it was from the distal rather than the proximal portion of the upper gastrointestinal tract.

DR. RUBNITZ: I will ask Dr. Gillesby to narrate a film that was taken in this case at the time of laparotomy.

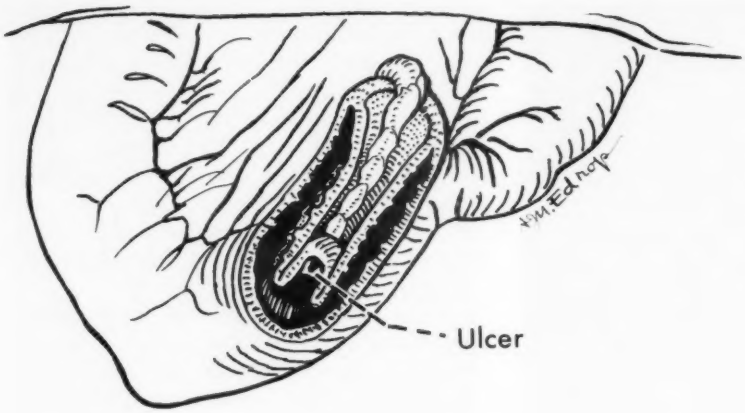

FIGURE 4. Intussusception of Meckel's diverticulum into ileum. Ulcer in aberrant gastric mucosa at tip.

DR. WILLIAM J. GILLESBY (assistant chief, surgical service): If you had seen these films before the arrows were put on, I can practically assure you that you would have missed the situation, but my own diagnosis was a leiomyosarcoma of the ileum.

Dr. Williamson used to say that when you hear *miaow* in the alley, it could be a lion escaped from the zoo, it could be a tiger escaped from a circus, but most likely it is just a plain old alley cat.

(A colored movie was shown for about eight minutes, demonstrating that this was an intussusception of a Meckel diverticulum into the ileum with gastric mucosa at the tip. Figures 4 and 5 were drawn from the film.)

Meckel's diverticulum was first described by Meckel from Halle, Germany, and I cannot give you the exact date; but it has been seen ever since, and the incidence is between 1 and 3 per cent, depending on how many one searches for. But I think the most important thing about Meckel's diverticulum is that in 10 per cent of the cases it is on the mesenteric side. If, in going over the bowel, you do it hastily, you can miss it very easily if it is tucked down on the side of the mesentery, away from the area where one usually looks for it. So here was a Meckel diverticulum that had gastric mucosa in it; gastric ulceration occurred and then intussusception, producing a polypoid mass.

At Hines, we have seen quite a number of Meckel's diverticula, and a fairly high percentage contained gastric mucosa. Two contained aberrant pancreatic tissue, and in both there was a little inflammation. There has been reported an acute hemorrhagic pancreatitis in aberrant pancreas in Meckel's diverticulum.

We have found duodenal mucosa, gastric mucosa and pancreas in these diverticula. I might say that in most of the cases we have seen, an appendectomy had been done at that horrible haven, "Elsewhere" Hospital, before the patients came to our hospital.

DR. RUBNITZ: Although we cannot point to any area as showing true gastric mucosa, parietal cells were seen, and it is our opinion that the ulceration was occurring in gastric mucosa but that as it regenerated it did not regenerate to gastric mucosa. But parietal cells were seen, so we have evidence that this was at one time gastric mucosa.

Dr. Gillesby, grossly you demonstrated a difference in the mucous membrane, and I wonder if, as it was regenerated, it regenerated to the original mucosa.

DR. GILLESBY: I do not know. From the standpoint of texture it is certainly different from the ileum as shown in the film.

There is one question I would like to ask. How can you explain relief of peptic ulcer by the ingestion of milk in a case of Meckel's diverticulum when the ulcer is 16 ft. away from where the milk is hitting? I have seen this happen rather frequently; they *do* get relief of ulcer pain.

DR. KAMMERLING: It is safer to say that the

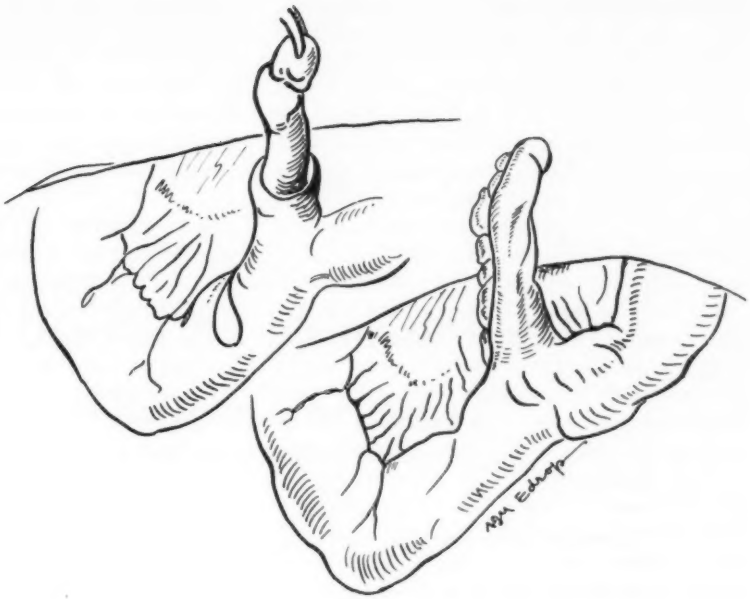

FIGURE 5. Intussusception reduced. Meckel's diverticulum on mesenteric side.

Figures 4 and 5 were drawn from a movie film made at the time of laparotomy.

pain was relieved *while* the patient was taking milk. Many times, patients with distal primary small-bowel ulcer may get relief but at the same time their dietary habits change; they are likely to go on a very soft bland diet in addition to taking milk, and at this distance from the stomach I do not see how milk or antacids would play a large part. But in patients with jejunal ulcer or primary ileal ulcer, an ulcer-type regimen may provide temporary relief.

DR. LITTMAN: I would like to try to answer this interesting and provocative question, starting back a bit further. The books say (and maybe some of us will live long enough to have this experience) that one can make the diagnosis of ulcer in Meckel's diverticulum by determining that the pain does occur in fixed relation to meals—usually three or four hours—and that antacids do *not* relieve the pain. That is the typical story of Meckel's diverticulum. Maybe this is what the resident was trying to tell us in recording the story. On the other hand, we do not customarily accept the word "griping" in reference to ulcer pain. We typically think of that as a disturbance of motility and normally think of griping in the epigastrium as being due to hyperperistalsis or partial obstruction in that area; we do not ordinarily think of griping pain as an ulcer-type pain. But typical ulcer pain is said to occur in a Meckel ulcer, with heterotopic gastric mucosa; however, typically the patients do *not* get relief.

DR. GILLESBY: That has been my reasoning. I do not think, *after* intussusception occurred, that the patient bled to an extent comparable to the previous episode, because the blood supply to this portion was definitely embarrassed. The neck of the diverticulum was quite hemorrhagic because of the length of time intussusception had been present. We know it was a generous length of time because we have x-rays which were made several days before.

DR. OSCAR HARMOS (staff physician, laboratory service): That reminds me of an autopsy in which I found three pigmented malignant melanoma nodes. One was in the brain, the second was in the upper lobe of the right lung, and the third was in a Meckel diverticulum.

DR. RUBNITZ: Three metastases in a case of melanoma, one of them present in a Meckel diverticulum.

The Physician, a Cultured Gentleman

PIERRHOS ST. KATSAREAS* AND FRIXOS X. COSTEAS†

University of Athens School of Medicine, Athens, Greece

Reverently dedicated to the memory of William Beaumont, an American Army surgeon

Scire potestates herbarum usumque medendi maluit et mutas agitare inglorius artes. It was his part to learn of the power of Medicine and of the manner of the healing and, heedless of glory, to exercise that quiet art. Virgil: Aeneid xii:396-397.

Let mee bee sicke myselfe, if sometimes the malady of my patient be not a disease unto me; I desire rather to cure his infirmities than my owne necessities. Where I do no good me thinkes it is scare honest gaine, though I confesse 'tis but the worthy salary of our well-intended endeavours.—Sir Thomas Browne.

PIERRHOS ST. KATSAREAS

FRIXOS X. COSTEAS

It has been a mark of the humanist since he began among us that "without deep love of humanity there could be no love of the Art." Although all of us would proudly heal and gladly learn, to be counted fit to heal is something of a crown to all men. Medicine has a glorious heritage and ranks as the most noble calling, whether to God or man, for, as the poet once said, "A physician is worth many other men."

In days of tribulation, patients will expect you to incorporate the offices of "scientist, healer, priest and prophet."[1] Conduct that shows understanding and sympathy for the feeling of others is the essence of good manners and good medicine. That is the practice of medicine as Hippocrates conceived it, and there was little in his Art that one would call "scientific." It is the practice of an Art, the highest exercise of which can come only from

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that imbued love for ideals and knowledge that is "like a light kindled by leaping fire"; of a Science, the cold logic of which keeps the mind independent and free from toils of self-deception and *hemimathia;* of a Charity that renders gentle hands and tender hearts and a "blessing which maketh rich and addeth no sorrow."

Plutarch said the life of a vestal virgin was divided into three portions: In the first she learned the duties of her profession, in the second she practiced them, and in the third she taught them to others. Thus, the establishing of a diagnosis, the planning of treatment, and the formulating of a prognosis must be learned from errors made, but there are a few hints which we may not be the worse for hearing.

The ancient's exclamation "I was born *to love* not to hate" constitutes the touchstone of success in medicine. The physician's sacred task is "to comfort always" (Trudeau), and, may we add, whenever possible to try to understand. It is not sufficient that the physician should believe he understands the patient; the patient must believe himself understood. In the Latin's more melodious phrase, "*Homo sum, humani nihil a me alienum puto*" (Terence). In this context *homo* includes both scientist and humanist, and *humani* means both human and humane. For the physician's humanity is that rare and noble kind which, in Emerson's words, "approves itself no mortal, but a native of the deeps of absolute and inextinguishable being."

Cultivate a spirit of fidelity and candor. Pithy language touches the heart. The most famous oracle of the ancient world issued such deceptive replies as "You will return not in battle will you die," leaving the vital punctuation up to the inquirer. Practice simplicity, with a dash of subtlety and independence.

Never think aloud before your patients. "The fairest thoughts," wrote Sherrington, "are the thoughts unspoken." And to preserve harmony in your associations with the sick, be a good listener, learn to stand by the bedside and make it your delight. Be careful what terms you mention around your patients; uncouth names of diseases should not come from a physician—they hang like an English fog over the patient's mind. Many of our noble aristocrats are less gentle and sympathetic than Eumaeus, the herdsman of Homer. Spare the sick person your ill-timed remarks. Mark you, the most important prescription you can ever give is *advice*. Do not be authoritative, or order your patients, "be it of virtue or of mischief," as Francis Bacon would have said. Grip your patients with friendliness, heal their mental hurts with sympathy, and give them the courage to carry on in life.

Do you recall the story of Oedipus? Like Laius, many a modern father has his son grow up a stranger to him, instead of helping the child to a mature upbringing. Plato's longing ἕνα γένεσθαι ἐκ πολλῶν might fittingly be chosen as the white stone of all healing work.

In the words of St. Paul, speak with the tongue of angels. Tell your patients a little story and let it convey its own message. And, in the quaint language of Sir Thomas Browne,[2] "allow one eye for what is laudable in them." Your whole experience of humanity must be focused on the individual patient. The physician must, as it were, "withdraw into the patient" with an infinitely delicate flexibility of soul which in Horderian elegance lifts up the weary head and comforts the sorrowing heart.

Always laugh *with* the patient, never *at* him. Avoid making light of any case. Guide the wanderer back to the straight path. "Many patients want the doctor to carry them back."[3] Make it a rule never to be angry at anything a patient does or says to you.

Learn to look *for* things, and soon you may discover that many patients hide their need with an ingenious brusqueness because they are just as much ashamed of their need as some of us may be of our power to supply it.[4] Perchance you recognize Penelope's web in the patient's attitude to illness; it is not impious to search diligently for apocryphal reasons.

In our younger days, when the stethoscope and the percussion hammer were peeping out of our coat pockets, we had many unhappy experiences with patients, and the foolishness of yesterday has taught us that what heals or injures has its cumulative effect in the region

of things inscrutable. It is the cultural and philosophical background of the cultivated gentleman of the type of Eryximachus that gives the physician dignity, social rank and respect. *Paideia*—medicine stands or falls by that. Men entrust to our care the perplexities not only of their bodies but also of their spirits, and these neither the products of test tube or crucible halts nor operations cure.

Protagoras held that "Man is the measure of all things," and Hippocrates studied "the whole man." The physician of old attempted to cure his patients and very often failed; the modern doctor attempts to cure disease in organs and frequently succeeds. The old practitioner never forgot that his patients were sentient human beings (a monarchy—the Hippocratic holistic approach). Learned in the wisdom of the sickroom, Sir William Gull said in a lecture to students that to give them an idea of Bright's disease he should have shown them not the patient's kidneys and heart in a bottle but the whole patient. *Ergo*, Hippocratism introduces more art and more science. It is thus pardonable for old men to look back nostalgically to horse-and-buggy days when the critical exercise of reasoning faculties was followed by manual examination aided only by a stethoscope.

There is the well-known story of Osler giving his cloak to a beggar, who in return bequeathed to "my friend William Osler" his liver, hobnailed by drink. Medicine cannot provide athanasia. We cannot cure all our patients but we may help them all. When such a man is about to die, he wears his fate like a royal robe, echoing Sophocles' Oedipus at Colonus: "I feel at peace now. It is the peace that ensues upon contrition when contrition ensues upon knowledge of the truth."

Loyalty and a profound belief in the gospel of the day's work were the texts from which the elders offered a distinct plan for life, including virtues to practice, knowledge to attain, graces to acquire; τό ἡγεμονικόν was their chief quality.

"I will keep pure and holy both my life and my art" (Hippocrates). Venerate and honor your colleagues. Judge not your confreres by the report of patients, well-meaning perhaps, but often strangely and sadly misinterpreted. Doctors' quarrels are about trifles and annoyances. Time will generally show that the words you would have spoken would have been unjust, would have injured a good man and lost you a friend—and, then, silence is a powerful weapon.

Respect your own profession! Beware of avarice, it hovers about this lower world and the earthly nature.

The chilling, killing isolation of the years amid the encroaching life of cities, hard routine and dry details sap the vitality of many who start with high aims—an ordeal which leaves none unscathed. Mark time in the "stand and wait" years. Faithfulness in the day of small things is the meaning and method in medical practice. "I have enduring faith in the men who do the routine work of our profession."[5]

"The successful physician starves the first ten years, lives on bread and butter the second, and may have cakes and ale the third decade" (Osler, 1897). Be an idealist; it minimizes the harsher features of life. Be a little proud—it will not hurt you.

Learn to know your colleagues and, like the Athenians at the Stoa, in the spirit of St. Paul, gather for "nothing else but either to tell or to hear some new things."

Consider the virtues of taciturnity. Commit yourself only when you can and must; when you speak, be laconic. Assert only that of which you know. Beware of words—they are dangerous things. If you are like Sydenham, "a man of many doubts," never make a "positive" diagnosis. And be on the lookout, for "many patients suffer from diseases which are not described in the textbooks."[6]

"The master word in medicine is Work" (Osler, 1903). Do the day's labor with closed lips; the deed in full measure will not be found in the record of man but recounted in "homely joys and destiny obscure" (Sir Thomas Browne).

Live in the ward and the outpatient clinic where your true love should be found. With constant contact with the sick, if you have but an impartial and honest mind you will discover that there are diseases and patients. Be

a pluralist: "Disease has a plurality of cures and a plurality of forms" (Hippocrates).

Method is the harness without which only the horses of genius travel. "Never ask a new patient a question without notebook and pencil in hand" (Osler, 1892). Beware of rejecting the facts of which you do not comprehend the import and because you do not comprehend it.

Like Astrophel, listen to nature's secret wonders. "Do not wait for fortune to smile on you; prepare yourself with knowledge" (Fleming, 1955). William Beaumont in the backwoods of America was quick to "grasp the skirts of happy chance."

Suppress your *alter ego* and never be ashamed of a healthy confession of error. To the brisk lad of ignorance learn to say "I do not know" and do not thumb, doubt and guess. Diffidence breeds inquiry. In the words of Hippocrates, "Science and opinion are two different things: Science is the father of knowledge but opinion breeds ignorance."

Possess a tranquil and kindly nature that irradiates the pleasant face it makes one happy to meet on his daily rounds. Try still to spend more time at the bedside—the biggest event in the patient's day.

"Make a habit of two things: To help or at least to do no harm" (Hippocrates). It is as important to know the *laedantia* as the *juvantia* in therapeutics. "It is not too late to *un*learn the habit of drugging for its own sake" (Holmes).

Like the uncertainty of a child who hesitates whether to creep safely on all fours or risk a fall by walking, be very slow in the presence of nature. "Nature herselfe must be our adviser; the path she chalks must be our walk" (Harvey). "Look and try for yourself" (Galen), and do not rely too much upon your results. You may have to be content only with the *Quia*. For "it is by your own eyes, and your own mind and (may I add) your own heart that you must observe and learn and profit."[7]

"Knowledge comes but wisdom lingers."[8] Spin from your own inward meditations your own mellowed learning. "Methods of work are learned from demonstration, methods of thought by conversation; communion inspires."[9] The practitioner lacks time for quiet thought. This was what Sir Thomas Browne felt when he wrote that his work had been composed by snatches of time from his practice, envying those whose "quiet doors and unmolested hours afford no such distractions." Leisure is a God-given gift.[10]

And if there be a higher source, as we trust there is, to which some of you have looked for the proper motives and destinies of man, and really know what they are, bring these and engage them in active exercise and link them to the great work of your lives. Then this keen joy in work will be exalted into a principle and, invested with a moral motive, slowly pass into the heart.

History has celebrated the humanitarian spirit of such men as Trousseau, Flint and Lister, and it was the great classic culture which gave these physicians that *esprit de finesse* so necessary for clinical observation and the power of logic so important for scientific work. "Woe to the day," said the philosopher Alfred Fouillée, "when physicians cease to constitute an intellectual elite." A knowledge of disease and its cure will make you a practitioner of medicine, and a knowledge of yourself may make you a truly good man, "foursquare and without a flaw" (Osler).

Only after years of experience, blunders immeasurable, chances lost forever by a single word said or unsaid, failures that were so nearly successes but for a method that was neglected or an assumption premature, humiliations, disappointments and misunderstandings, only then do we begin to grow mature in human life and affairs. "How crude we are at first, and how clumsy even at the last!" (Horder, 1936).

We are not perfect, nor do all of us live up to the highest ideals, but if we err let our faults be mistakes of the head, not of the heart. We believe in ideals which are ever old yet always fresh and new, for we have learned from the past that it is not by the removal of obstacles that man progresses, but it is through the courage to overcome them. It ill becomes us to forget the peasant who, so weary of hearing Aristides always called The Just, gladly took up the oyster shell for his ostracism and

even asked Aristides himself, whom he did not know, to mark it. For where the climate is severe, Hippocrates wrote, the people are "hard, stubborn and independent."

It is not life that is the highest call but the way of life and the faith we bring to it; *ignes fatui*, a man's life is not what he reads or what he has accomplished, but his inclinations and aspirations, his inner life.

As Sir Thomas Browne, most liberal of men and most distinguished of general practitioners, so beautifully remarked: "While thou so hotly disclaimest the devil, be not guilty of diabolism. Fall not into one name with that unclean spirit, nor act his nature whom thou so much abhorrest—that is to accuse, calumniate, backbite, whisper, detract, or sinistrously interpret others. Degenerous depravities, and narrow-minded vices! Not only below St. Paul's noble Christian, but Aristotle's true gentleman. Trust not with some that the Epistle of St. James is apocryphal, and so read with less fear that stabbing truth, that in company with this vice thy religion is in vain. Moses broke the tables without braking the law; but where charity is broke the law itself is shattered, which cannot be whole without love, which is the fulfilling of it. Look humbly upon thy virtues; and though thou art rich in some, yet think thyself poor and naked without that crowning grace, which thinketh no evil, which envieth not, which beareth, hopeth, believeth, endureth all things. With these sure graces, while busy tongues are crying out for a drop of cold water, mutes may be in happiness, and sing the *Trisagion* in heaven."

It was not Browne's intent to purge the Augean stables but to bring out the *beau ideal* in the physician's character. For in no other profession does culture weigh for so much as in medicine, and no one values it more than the cultivated general practitioner, whose Art in life is to know disease and to know how to treat patients. "He is a gentleman in character, and being this he is grave and kind to all" (Hippocrates).

Medicine is an exact science, and the life devoted to science is a sacrifice. The dictum put into the mouth of Ulysses, "I am part of all that I have met," expresses the truth of the influence of the elders on their pupils, and it is of our learned teachers that we are thinking when we conclude with the words of the poet-physician Sherrington: "The only reality is the human soul. Keep on struggling for the reality of the spirit. It is something the world needs." *Vivitur ingenio, caetera mortis erund.* What lives is the spirit, all else belongs to death (Andreas Vesalius).

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Self-help Devices:

Aids to Telephoning

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Reaching for, Grasping and Maintaining Hold on Handset

FIGURE 1. The telephone rests on a metal stand that has an upright rod with a swivel attachment to which the handset may be permanently fastened. The handset can be adjusted to the user's convenience; however, it is necessary to remove and replace a telephone guard, weighing about 10 oz., to open and close the circuit.

J. A. Preston, 175 Fifth Avenue, New York 10. State type of telephone on which unit is to be used. $10.95 with telephone guard.

FIGURE 2. The Phone-Mate has a gooseneck attachment that provides a considerable degree of adjustability. An upward flip of the conversation key prepares the telephone for dialing; a downward flip of the key breaks the connection.

Fascole, 257 Park Avenue South, New York 10. $9.25, shipping and handling $0.75 extra.

*Supported at the Institute by the Arthritis and Rheumatism Foundation.

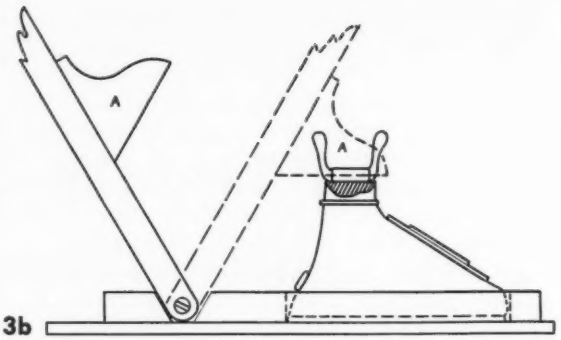

FIGURE 3. a. This unit, designed by C. B. Snodgrass, is not commercially available. However, it can be easily duplicated by anyone who has some skill in carpentering. A movable upright arm supports the telephone mouthpiece. A horizontal wedge (A in b) on the back of the upright arm holds down the switch bar. To disengage the switch for dialing, the movable arm is pulled away from the telephone.

Prolonged Holding of Handset

FIGURE 4. a. The Tele-Rest, which is made of molded black TENITE®, has a clamp band that fits any telephone and has a rubber-cushioned shoulder cradle. It is adjustable to either ear and is especially useful for persons who have only one functioning upper extremity, because it releases the "good" hand for dialing and taking notes.

Local gift and stationery shops, hardware stores, Fascole and J. A. Preston. About $2.00.

b. Telephone companies have a cradle device that is incorporated permanently onto the handset and is shaped to shoulder contour. See local telephone company for cost of installation.

FIGURE 5. Several dialers can be purchased or home-devised to eliminate the necessity of inserting the fingers directly into the dial slots. This device from Breck's, Boston, has three initials engraved on the handle. $1.50.

Less expensive devices can be purchased from most local stationery and gift shops and hardware stores. A pencil is often a good substitute.

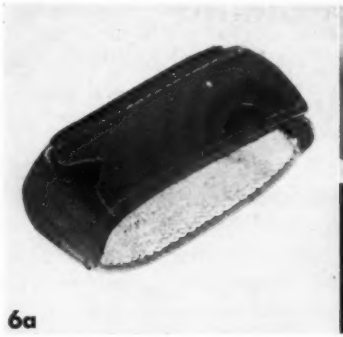

FIGURE 6. a and b. Those whose poor grasp or painful or weak fingers prohibit use of an upright dialer may be able to dial successfully by using the Utensil Holder combined with a dialer. Fascole. $1.00.

FIGURE 7. a and b. This unit was designed at the Device Shop of the Institute of Physical Medicine and Rehabilitation for persons with severe arthritic involvement of the hands. A cuff is made by attaching an elastic strap to a piece of dowel that is large enough to fit over the palmar surface of the hand. In this instance, an aluminum dialer is inserted into the dowel at a right angle.

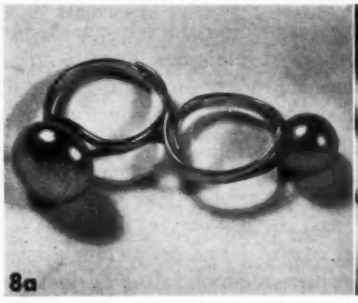

FIGURE 8. a and b. Submitted by Dr. Camille K. Cayley, this dialer consists of two Mexican silver rings soldered together but not closed, to allow for variable swelling of the fingers. Worn on the fourth and fifth fingers, the circlet on the fourth finger stabilizes the functioning half on the fifth finger. The silver bead extends freely from the ulnar side of the hand and is sized to fit into the dial slots.

The rings can be obtained from local jewelry or novelty stores.

Readers are invited to submit suggestions and ideas for devices they have developed and would like to share with others. Forward all such suggestions and comments to: Editorial Department, POSTGRADUATE MEDICINE, Essex Building, Minneapolis 3.

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INFECTIOUS HEPATITIS

When, during World War II, infectious hepatitis (or infectious jaundice) occurred in epidemic proportions among personnel of the Armed Forces, some clarification of its etiology, epidemiology and natural history was achieved. By no means, however, is infectious hepatitis a closed chapter of medical knowledge. Successful prevention of this disease must await the attainment of more fundamental facts in its epidemiology.

It seems likely that infectious hepatitis is an extremely common childhood infection, often anicteric and of low morbidity, transmitted by the intestinal-oral route. The finding of the virus in the stool and in the blood as long as two or three weeks before the onset of jaundice presents problems in the prevention of spread of this infection. How long the virus may continue to be excreted in the stool after the onset of jaundice is unknown, but the time probably is not uniform. Variations in the incubation period of the disease when studied in human volunteers and the occasional occurrence of reinfection suggest the existence of multiple strains of the virus.

It is truly remarkable that so much knowledge of the epidemiology of infectious hepatitis has been gained by careful clinical studies of naturally occurring epidemics and by the use of human volunteers. Despite failure to culture the viral agent of infectious jaundice or to transmit the infection to any laboratory animal, progress continues to be made in its epidemiology and prevention. Ward, Krugman and Giles,[1,2] who have contributed significantly to this progress, review current concepts of the epidemiology and prevention of infectious hepatitis in this issue of Postgraduate Medicine.*

At a very practical clinical level, sporadically occurring cases of infectious hepatitis may present significant problems in the differential diagnosis of jaundice. Variations in the clinical history, physical findings and course of infectious hepatitis may tax the most astute clinical judgment. It probably is safe to predict that, in arriving at a correct diagnosis in the individual case of jaundice, no single laboratory test will soon supplant the evaluation of a carefully taken history and a thorough physical examination. Hence familiarity with

*Page 12.

the symptomatology and the vagaries of the course of infectious hepatitis are incumbent on physician and surgeon alike.

Laboratory aids in the diagnosis of infectious hepatitis are indeed most helpful when properly applied and properly interpreted. The so-called flocculation tests of liver function have proved their worth in wide application through some 15 years. More recently determinations of serum enzymes have been applied with considerable usefulness to the differential diagnosis of jaundice. The most widely used of the enzyme tests has been the determination of serum transaminases. Wróblewski[3] has clearly demonstrated the value of the serum transaminase level in the diagnosis of acute hepatocellular disease. Other familiar and older laboratory tests of liver function still have a place in the diagnosis of infectious hepatitis, even though at times their results may be meaningful primarily in a negative sense. Always, however, it must be remembered that no specific laboratory test for infectious hepatitis exists. Even the histologic findings in needle biopsy specimens from the liver are not absolutely diagnostic of infectious hepatitis.[4] To consider the histopathologic finding of postnecrotic cirrhosis as always indicative of prior infection with the virus of infectious hepatitis seems even less justifiable.

Although no specific therapy for viral hepatitis is available, questions persist regarding the application of nonspecific therapeutic measures: The value of strict rest in bed, how long such a regimen should be persisted in, and what criteria should be used to determine when to begin ambulation are all topics of some continuing controversy. Certainly ideas relating to the use of bed rest and ambulation in the treatment of infectious hepatitis have been modified in the past 10 years. Concepts of dietary therapy also have been altered, and the use of steroids in the therapy of this disease remains controversial. Subsequent articles in this journal will deal with the diagnosis and treatment of infectious hepatitis.

The incidence of chronic liver disease has been increasing rapidly in the United States in the past decade, as measured by morbidity and by mortality. Although follow-up studies of service personnel who contracted infectious hepatitis during their period of service have failed to show an increased incidence of subsequently developing cirrhosis,[5] other studies among civilian groups indicate that infection with the virus of hepatitis may lead to serious chronic liver disease.[6] The severity of acute infectious hepatitis is known to be increased among adults and seems to be greater in women than in men. Serious chronic complications of acute infectious hepatitis seem to develop more readily in females than in males.

To determine whether acute hepatitis is related to chronic liver disease and, if such a relation exists, the factors responsible for chronicity—including possible hormonal influences—will require much further study. The development of a specific test to demonstrate infection with the virus or viruses of infectious hepatitis and of methods for culturing and transmitting these agents to a laboratory animal is desirable. With such tools, answers should be found for the many questions that still exist regarding the epidemiology, diagnosis and therapy of the disease as well as the significance of this infection in the subsequent development of serious chronic liver disease.

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EARLY DEVELOPMENT OF GALLBLADDER SURGERY

On October 17, 1859, Dr. J. L. W. Thudichum addressed the Medical Society of London on "The pathology and treatment of gallstones." He recommended operating on the gallbladder in gallstone disease and also described a technic which involved making an incision large enough to admit the forefinger in order to explore the gallbladder for the presence or absence of calculi. He proposed if calculi were present to pull the gallbladder into the abdominal wound and fix it there without opening it. Then he said, "In six days a good and passable fistula will be established, which, after a fortnight or three weeks, will be sufficiently consolidated to admit of the introduction of an instrument, by which such soft calculi may easily be crushed."

His proposal attracted little attention until eight years later. On June 15, 1867, John Stough Bobbs, Indianapolis, operated on a woman thought to have an ovarian tumor. According to Dr. Robert S. Sparkman,[1] the mass proved to be a huge hydropic gallbladder. Many stones and much fluid were removed, and the opening in the gallbladder was closed. This patient survived and, indeed, attended a meeting of the American Medical Association 37 years later.

The first *premeditated* operation on the gallbladder was performed by J. Marion Sims on April 18, 1878. Theodor Kocher, Bern, Switzerland, did a gallbladder operation on June 18, 1878, and W. W. Keen, Philadelphia, operated on the gallbladder on November 4, 1878. The fifth recorded operation was performed by Mr. Lawson Tait of England and was reported November 11, 1879. In his essay on the subject, Dr. Sparkman gives succinct descriptions of these operations and their results.

Dr. Sparkman, who is attending surgeon at Baylor University Medical Center, has reviewed this evolution of gallbladder surgery as a recognition of its centenary. Thudichum, who apparently was the first to perform such an operation, wrote little about the gallbladder thereafter, although he did propound the nidal theory for the formation of gallstones in a text published in 1863. Although his name is seldom mentioned in the annals of surgical history, Thudichum wrote authoritative works on many subjects, including the chemistry of wine and beer, cookery, otolaryngology, public health, and industrial medicine.

Dr. Sparkman noted that in 1953 the State Research Hospital for the mentally ill, Galesburg, Illinois, dedicated a psychiatric research laboratory as the Thudichum Laboratory; an annual Thudichum Lecture has been initiated there. The most monumental contribution of Thudichum was a study of the chemistry of the brain, and it was this research that brought the recognition given in Illinois.

MORRIS FISHBEIN

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THE SANATORIUMS FOR TUBERCULOSIS

During 1956 there were 14,061 deaths from tuberculosis and 68,866 new active and probably active cases reported. Authorities estimate that 400,000 people with tuberculosis are under the supervision of local health departments. Of these, about 150,000 are considered to have active tuberculosis and 250,000 inactive tuberculosis. Estimates also indicate another 400,000 cases of tuberculosis which should probably be under public health supervision but which have not come to public attention. Notwithstanding the scope of these statistics, the rate of decline of deaths from tuberculosis has been greater in recent years than ever previously. Newly reported cases have not declined as rapidly as has the death rate. The introduction of new remedies, such as streptomycin, para-aminosalicylic acid and isoniazid, has brought about this tremendous revolution in the care of tuberculous patients and has resulted in a pressing problem for all the sanatoriums. In the early 1900s tuberculosis was the leading cause of death, with a rate approximating 200 for 100,000 popula-

tion. In late 1958, the rate had dropped to eight per 100,000 population. There are many states with death rates below five per 100,000.

To quote Dr. Louis I. Dublin, "The balance between the tubercle bacillus and man has finally given way in favor of man .... We cannot say exactly when control will be complete, but there is every indication that it will be sometime in the course of the next 20 years."

In the great campaign against tuberculosis which marked the first half of this century, sanatoriums were built throughout the United States under local, county, state and national sponsorship, and many private institutions were made available to those with adequate funds. The gradual decline in the need for sanatoriums has resulted in problems for the sponsors, the boards of directors, and the various agencies established to accumulate funds in support of these institutions. The Municipal Tuberculosis Sanitarium in Chicago, which formerly had a waiting list of several thousands, now finds itself without a waiting list and able to accommodate patients formerly given care at the Cook County Hospital. Many patients with tuberculosis can be treated with the new drugs, be made free from the hazard of distributing germs, and receive their treatment as outpatients in dispensaries.

As a result of these changes, the institutions formerly devoted to tuberculosis have become available for other purposes. Some have been adapted to the care of the aged and the infirm. Others have changed the focus of their attention from tuberculosis to other chest diseases, to asthma, to cystic fibrosis, and to cardiac surgery. Still others are being sponsored as institutions for both basic and applied medical research. The fund-raising organizations with facilities and chapters scattered throughout the United States feel that their continuance is desirable since there still remain many medical problems to be solved. The Jewish Consumptives Relief Society, which maintained extensive facilities in Denver, has turned its attention to the care of patients with cancer. Its great Texas Pavilion, formerly devoted to the care of women with tuberculosis, is now wholly occupied by patients with terminal cancer. Here, funds are being raised to build a cancer research institute which will bear the name of Mrs. Eleanor Roosevelt. Another institution is devoted to the care of children with asthma and still another has become an institution for the care of mild mental cases.

Here is a national problem for which no attempt has been made at an orderly scientific solution. Conceivably, some leading health agency, such as the National Institutes of Health or the National Health Council, could by a suitable conference work out a more scientific evolution of these institutions.

MORRIS FISHBEIN

THE SECRET OF THE MONA LISA

LEONARDO da Vinci is recognized throughout the world as a great painter, a scientist, an anatomist and a writer. The Mona Lisa is undoubtedly the most widely known of all his paintings. Giorgio Vasari said, "For Francesco del Giocondo Leonardo undertook the portrait of Mona Lisa, his wife, and left it incomplete after working at it for four years." She was married at 16 in 1495, becoming the third wife of Del Giocondo, one of the great persons of Florence. Mona Lisa sat for her portrait intermittently for four years. She was 21 when Leonardo first saw her; she had already lost a small daughter. Physicians are interested primarily because there is now a debate as to whether or not she was pregnant when the portrait was painted.

In a paper presented before the Beaumont Medical Club of New Haven, Kenneth D. Keele,[1] visiting professor of the history of medicine at Yale University School of Medicine, spoke of "The genesis of Mona Lisa," presenting facsimiles of some of the famous sketches in the notebooks and having much more to say about Leonardo da Vinci than about the Mona Lisa.

The descriptions of the Mona Lisa usually describe her as placid or tranquil rather than as a woman with feminine allure. One can be sure that she was not anemic. Vasari refers to the possibility that she may have had an enlarged thyroid. Many of those who have commented on the picture refer to the puffiness of

the cheeks. The quizzical smile has been described as not a smile of joy or charm or love but "a mantling disguise for a deeper-lying feeling which must not be betrayed." A woman critic felt that Leonardo was by no means in love with Mona Lisa and says "that she is enchanting but disenchanted," and this Rachel Annand Taylor says "is the disenchantment of every woman who has found love's consummation destroys the rare pattern of her illusion." Another critic has said that Mona Lisa was like the mother with whom Leonardo fell in love as a child.

Keele said that few previous portraits of pregnancy had been made "and women do not usually choose that period of their lives for their portraits." He stated that "the difficult aesthetic problem of harmonizing the disproportions of pregnancy, and presenting it as the beautiful process he saw it to be, was solved by Leonardo in the simple half-turn of Mona Lisa's body, the arm being brought across the big belly and the hands lightly crossed on the arm of her chair."

Sir Kenneth Clark described the smile of Mona Lisa as "something worldly, watchful, and self-satisfied," which may also well be used to describe a pregnant woman.

Sigmund Freud described the smile by saying, "Her smile fascinated the artist no less than all the spectators for these 400 years. He found this smile in his model and became so charmed by it that from now on he endowed it on all the free creatures of his phantasy." Freud believed that Leonardo had a mother fixation and it was because of this that he chose Mona Lisa as his model. Walter Pater wrote that "a feeling for maternity is indeed always characteristic of Leonardo."

Most likely the secret of the Mona Lisa smile or even whether or not she was pregnant will never be solved. For 450 years this portrait has presented a diagnostic problem. The view of Keele that she was pregnant has much to be said in its behalf.

MORRIS FISHBEIN

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ATHEROSCLEROSIS IN ANCIENT EGYPTIAN MUMMIES

In an ancient Egyptian tomb of the sixth dynasty, about 2500 B.C., appears a drawing which medical experts feel is probably the first depiction of a man dying from coronary thrombosis. The picture shows him semiprostrate while two attendants try to help him, one holding a hand to the forehead, a gesture used by the Egyptians to express despair. In the second section of the picture the wife, apparently terror-stricken, has fainted and sunk to the floor and she is being assisted by two servants. This picture if in modern clothing could easily be the scene in many households of the present day when someone is stricken with coronary thrombosis or what is commonly called a "heart attack."

The paleopathologists who have examined the mummified bodies of various Pharaohs report that the body of Menephtah, who was Pharaoh at the time the Hebrews left Egypt in the Exodus, displayed severe atherosclerosis. This mummy was unwrapped by the archeologist G. Elliot Smith, who sent a piece of the Pharaoh's aorta to Dr. S. G. Shattock of London in 1908. Since that time Sir Marc Armand Ruffer of the Cairo Medical School, one of the most distinguished of all paleopathologists, has reported many other mummies with severe atherosclerosis. Indeed, Ruffer states that arterial lesions similar to those found by modern pathologists caused as much suffering among the Egyptians of ancient times as in modern man. One wonders about the Egyptians' cholesterol.

Dr. Walter L. Bruetsch[1] concluded from a review of writings in this field that the sudden death in the tomb of an Egyptian nobleman described in a book by F. W. von Bissing is presumptive evidence of sudden death caused by atherosclerotic occlusion of the coronary arteries.

MORRIS FISHBEIN

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in cirrhosis with ascites

"All three of the patients with Laennec's cirrhosis, ascites and edema had a favorable response, with a mean weight loss of 8 lbs., during the five-day treatment period with a slight decrease in edema." Castle, C. N., Conrad, J. K. and Hecht, H. H.: Arch. Int. Med., **103**:415, (March) 1959.

in renal edema

"In a study of 10 patients with the nephrotic syndrome associated with various types of renal disease, orally administered chlorothiazide was a successful, and sometimes dramatic, diuretic agent." Burch, G. E. and White, M. A., Jr.: Arch. Int. Med., **103**:369, (March) 1959.

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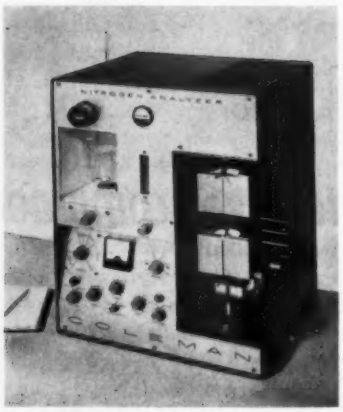

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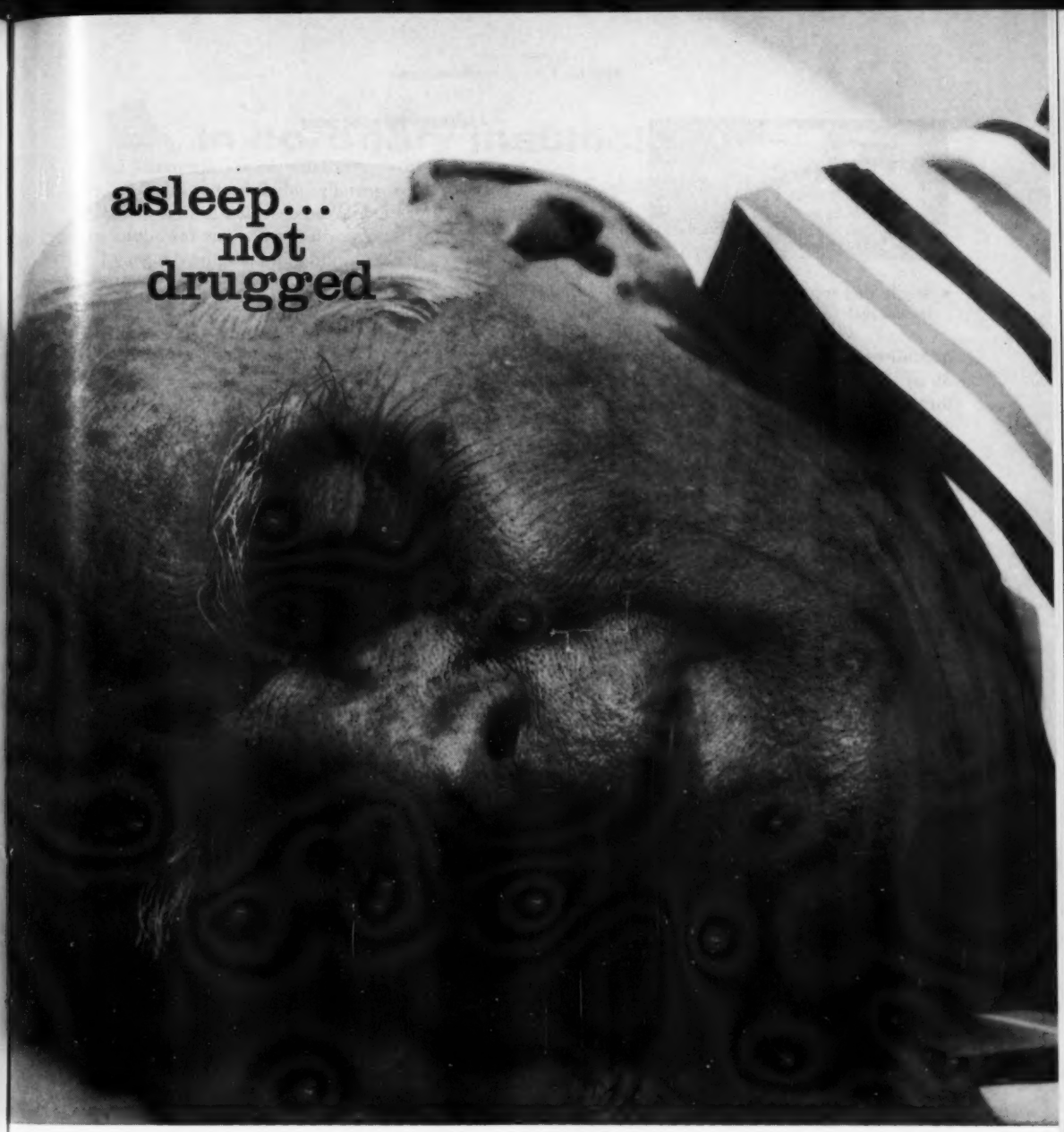

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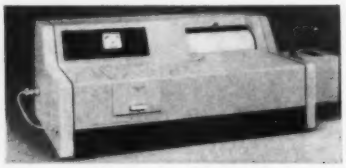

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PRODUCER: The Victoreen Instrument Company, Cleveland.

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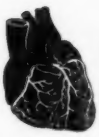
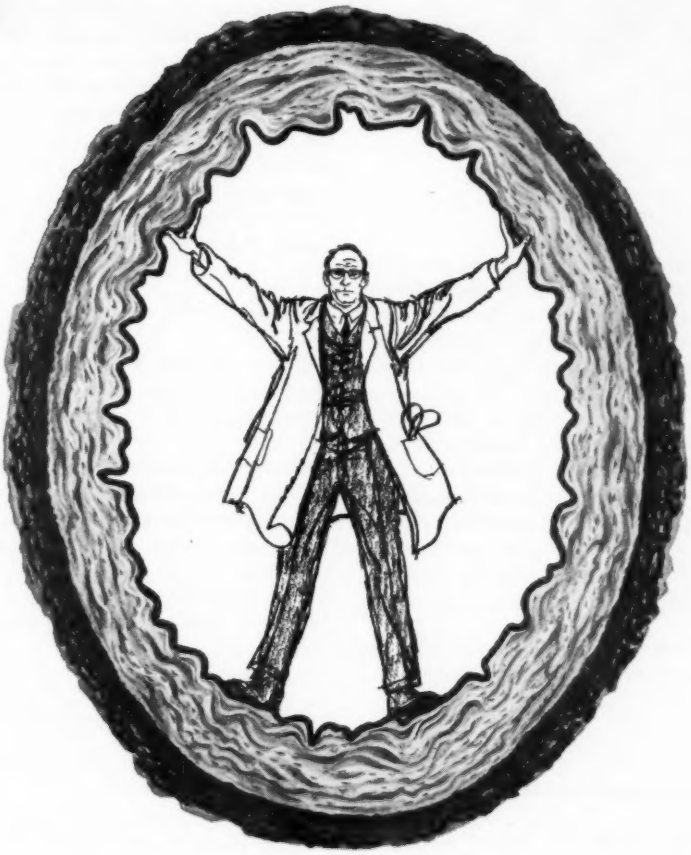


in coronary insufficiency



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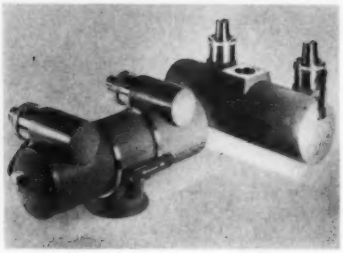

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Vitamin A (synthetic)	1.5 mg. (5000 U.S.P. units)
Vitamin D	25 μg. (1000 U.S.P. units)
Vitamin C	50 mg.

The Polyvitamin Drops and the orange-flavored Pediatric Syrup each contain eight vitamins.
DOSAGE AND ADMINISTRATION: ADC Drops and Polyvitamin Drops: 0.6 cc. or as prescribed. Pediatric Syrup: 1 to 2 teaspoonfuls daily in proportion to age and weight.
HOW SUPPLIED: ADC Drops and Polyvitamin Drops: 15 and 50 cc. bottles, with a calibrated dropper. Pediatric Syrup: 8 oz. aerosol cans.
PRODUCER: Merck Sharp & Dohme, division of Merck & Co., Inc., Philadelphia.

• ALPEN®

PURPOSE: Antibiotic therapy.
COMPOSITION: Potassium phenethicillin.
DOSAGE AND ADMINISTRATION: 125 or 250 mg. three times daily. In more severe conditions, 500 mg. three times daily may be advisable.
HOW SUPPLIED: 125 and 250 mg. tablets in bottles of 25 and 100. Also available as a powder for oral solution providing 125 mg. Alpen per teaspoonful.
PRODUCER: Schering Corporation, Bloomfield and Union, N. J.

• NICALEX

PURPOSE: To treat hypercholesteremia.
COMPOSITION: Each tablet contains 625 mg. aluminum nicotinate, equivalent to 500 mg. nicotinic acid.
CAUTION: Patients with peptic ulcer or disease of the liver or gallbladder should be closely observed during treatment.
DOSAGE AND ADMINISTRATION: 2 to 4 tablets three times daily.
HOW SUPPLIED: Bottles of 100.
PRODUCER: Walker Laboratories, Inc., Mount Vernon, N. Y.

• QUINOLOR® COMPOUND OINTMENT

PURPOSE: Antiseptic agent for superficial skin lesions.
COMPOSITION: 0.5 per cent chlorhydroxyquinoline and 10 per cent benzoyl peroxide in Plastibase, an ointment base containing liquid petrolatum polyethylene.
HOW SUPPLIED: 1 oz. tubes and 1 lb. jars.
PRODUCER: E. R. Squibb & Sons, division of Olin Mathieson Chemical Corporation, New York.

• FERRONORD® PROGRAVA

PURPOSE: Iron therapy during pregnancy and lactation.
COMPOSITION: Each capsule contains a phosphorus-free vitamin and mineral dietary supplement, ferroglycine sulfate complex, and 0.2 mg. folic acid.
HOW SUPPLIED: Bottles of 90.
PRODUCER: Nordson Pharmaceutical Laboratories, Inc., Irvington, N. J.

1960
Interstate Postgraduate Medical Assembly
Pittsburgh, Pa., October 31–November 3

ROBERT M. ZOLLINGER

Dear Doctor:

Since World War II there has been an expansion of medical postgraduate education which poses a problem for the conscientious physician who wishes to keep abreast of new developments in medical science. Without exaggeration, it is safe to state that any physician who wishes to take advantage of the many fine meetings which offer instruction might well spend his entire life in learning, with no time left to apply his knowledge to patient care!

In all this new development in postgraduate medical education, the wise physician must carefully pick and choose meetings which offer him the greatest amount of quality instruction within the shortest period of time. For the average physician who does not devote his practice to a single specialty, the Annual Assembly of the Interstate Postgraduate Medical Association has much to offer. If you have not yet attended one of these fine meetings, I invite you to do so when the 45th Annual Scientific Assembly is presented at the new and beautiful Pittsburgh-Hilton Hotel in Pittsburgh, Pennsylvania, October 31 to November 3. It has been my privilege to take part in many of these Assemblies in the past, and as a teacher I regard it as one of the most satisfying experiences I enjoy. This year, as President of Interstate, I have a special pride in the high-quality program which the Trustees have arranged, and I am sure that you would find it a program of great practical value.

Many outstanding medical teachers are contributing their time and talents to this four day lecture and discussion program. I am sure that if you attend, you will feel that the time spent is very worthwhile.

Sincerely yours,

Robert M. Zollinger

Robert M. Zollinger, M.D.
President

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION 45th SCIENTIFIC ASSEMBLY

Pittsburgh Hilton Hotel
Pittsburgh, Pennsylvania
October 31 – November 3, 1960

MONDAY, OCTOBER 31

MILTON L. McCALL, M.D., Pittsburgh
Prof. & Chr., Dept. of OB & GYN, Univ. of Pittsburgh School of Medicine
"Toxemias of Pregnancy"

FREDRICK J. STARE, M.D., Boston
Prof. of Nutrition, Harvard Medical School
"Nutrition in Relation to Arteriosclerosis"

RICHARD V. EBERT, M.D., Little Rock, Ark.
Prof. & Head, Dept. of Medicine, Univ. of Arkansas School of Medicine
"Pulmonary Emphysema"

OVID O. MEYER, M.D., Madison, Wis.
Prof. & Chr., Dept. of Medicine, Univ. of Wisconsin Medical School
"Newer Drugs and Their Uses"

E. RICHARD HARRELL, M.D., Ann Arbor
Assoc. Prof. of Dermatology, Univ. of Michigan Medical School
"The Treatment of Superficial Fungus Infections"

FRANK H. MAYFIELD, M.D., Cincinnati
Asst. Prof. of Clinical Surgery, Univ. of Cincinnati College of Medicine.
"The Diagnosis and Treatment of 'Whiplash' Injuries"

T. T. MYERS, M.D., Rochester, Minn.
Section of Peripheral Vein Surgery, Mayo Clinic
"The Continuing Problem of Varicose Veins"

WILLIAM MALLINSON McISAAC, M.D., Ph.D., Cleveland
Research Division, Cleveland Clinic
"A Biochemical Concept of Mental Disease"

NORMAN O. ROTHERMICH, M.D., Columbus
Clin. Assoc. Prof. of Medicine, Ohio State Univ. College of Medicine
"Intra-Articular Use of Steroids"

RICHARD E. STRAITH, M.D., Detroit
Straith Clinic
"Plastic Wound Closure"

Evening Program

ORTHOPEDIC CLINIC:
A coordinated program of demonstrations and informal lectures by Albert B. Ferguson, Jr., M.D., and William F. Donaldson, M.D., and associates, Pittsburgh

DERMATOLOGY "WET CLINIC":
Case presentations by Townsend Baer, M.D., and associates, Pittsburgh. (E. Richard Harrell, M.D., consultant)

TUESDAY, NOVEMBER 1

WILLIAM H. ZINKHAM, M.D., Baltimore
Asst. Prof. of Pediatrics, Johns Hopkins Univ. School of Medicine
"Drug Induced Hemolytic Anemias"

MICHAEL E. DE BAKEY, M.D., Houston, Texas
Prof. of Surgery, Baylor Univ. College of Medicine
"The Clinical Significance of Atherosclerotic Occlusive Disease"

SAMUEL P. HARBISON, M.D., Pittsburgh
Prof. & Chr., Dept. of Surgery, Univ. of Pittsburgh School of Medicine

MICHAEL E. DE BAKEY, M.D., Houston, Texas
Prof. of Surgery, Baylor Univ. College of Medicine

CAMPBELL MOSES, M.D., Pittsburgh
Assoc. Prof. of Medicine and Director, Addison H. Gibson Laboratories, Univ. of Pittsburgh School of Medicine
"Peripheral Arterial Diseases" (Panel)

CURTIS J. LUND, M.D., Rochester, N.Y.
Prof. of OB & GYN, Univ. of Rochester School of Medicine
"The Use of Cervical Cytology, Biopsy and Conization"

THADDEUS S. DANOWSKI, M.D., Pittsburgh
Prof. of Clinical Research, Univ. of Pittsburgh School of Medicine

STEFAN S. FAJANS, M.D., Ann Arbor, Mich.
Assoc. Prof. of Internal Medicine, Univ. of Michigan Medical School

LELAND S. McKITTRICK, M.D., Boston
Clinical Prof. of Surgery, Emeritus, Harvard Medical School
"Diabetes Today: Medical and Surgical" (Panel)

JONAS E. SALK, M.D., Pittsburgh
Prof. of Preventive Medicine, Univ. of Pittsburgh School of Medicine
"Virus Diseases—Their Control by Immunologic Means"

LELAND S. McKITTRICK, M.D., Boston
Clinical Prof. of Surgery, Emeritus, Harvard Medical School
"Carcinoma of The Colon; Difficulties in Diagnosis; and Principles of Treatment"

FRANK P. FOSTER, M.D., Boston
Department of Medicine, Lahey Clinic
"Some Elements Essential to Success in The Care of Serious Infections"

Evening Program

Two-hour concert of Slavic music and dancing by the world-famous "Tamburitzans" of Duquesne University. Special price of $1.00 per person (other costs underwritten by Interstate). Tickets available at time of registration. Distinctive entertainment of a quality nature, and reflecting the old-world culture of the Pittsburgh area. Plan to attend!

ADVANCE REGISTRATION: Send directly to Dr. E. R. Schmidt, 1109, Madison 1, Wisconsin. Registration fee: $10.00. Breakfast conference fee: $3.00 (see page 24 and list three in order of preference).

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JULY 1960

If You Live In An Apartment - it's advisable to insure the premises against fire, theft, negligent law suits, and other hazards. A leading real estate broker recently pointed out that apartment dwellers generally are less alert than home owners in realizing the need for such protection.

If a local tradesman, household employe, or visitor is injured in a public hallway as a result of landlord's negligence, you are not liable for any damages. However, if the same accident occurred in your apartment, you would be liable. Any damages in such case would come out of your pocket. On purchase of insurance covering your apartment, consider coverage under a comprehensive policy. It could produce premium savings. For instance, a policy giving a tenant $1,500 theft coverage, $5,000 fire insurance, $10,000 in liability plus related coverage might cost $140 for three years. Premium on this policy would run 20% less than the cost of buying three types of coverage separately.

Unless the visitor injured in your apartment was a patient calling upon you for professional services, it's unlikely that any damages you pay would give tax deduction. Damages would have to come out of your after-tax income. As a general rule, premiums you pay on an insurance policy as protection against such personal injury claims also would not be deductible. However, at a comparatively modest cost, you could secure coverage up to $10,000.

There Are Styles In Jewelry - which may change with the times. If jewelry you gave your wife is dated by a change in style, you might keep a recent Internal Revenue Service concession in mind. When you purchase jewelry, a Federal excise tax will be levied on the purchase price. However, that tax doesn't apply to jewelry already owned by a customer. If your wife wishes to have an old-fashioned ring restyled, the charge a jeweler makes for his labor is not subject to the excise tax. That means a saving for you.

* * * * *

Timber Is A Tax-Sheltered Investment - which has attracted the attention of big investors because of optimistic long-term forecasts for wood-fiber products. However, comparatively few investors have the capital or time to supervise direct investment in timber holdings. As an alternative to direct investment in timber holdings, one leading brokerage house suggests exploring investment potential of wood-fiber company stocks. It used Georgia-Pacific Corporation as an example.

When a wood-fiber company cuts timber it owns, it can treat the cutting as a taxable event. It reports the difference between its tax cost for the timber and current market value as a capital gain profit. The company doesn't pay full corporate tax on such difference. However, when it uses the cut timber in its manufacturing operations, it takes market value in figuring its selling costs. The tax effect is to reduce manufacturing profits which it must report and which are taxable at a 52% rate - at the expense of a 25% capital gains tax. If a company has extensive timber holdings with a low-tax cost, the corporate tax it pays on manufacturing profits may run considerably less than the usual 52% rate. In recent years, Georgia-Pacific has paid corporate taxes at a rate of around 30%. If the company can put those tax savings to profitable use, earnings for the benefit of stockholders will climb. In the past, that has been reflected in rising profits for Georgia-Pacific. Net earnings rose from 21¢ a share in 1953 to $2.58 in 1959.

A Tax-Exempt Income Return On Investment - may be extremely important to the successful professional man. He can't tax protect earnings from his practice so he must seek tax shelter on income received from investments.

If you seek tax-exempt income from a bond which offers maximum safety, you might investigate the return available from those issued by public housing authorities. The interest on such bonds is exempt from Federal income tax. In addition, all these bonds are backed with a U.S. guarantee as to interest and principal. For higher tax-exempt return, you might consider housing authority bonds issued by smaller communities first.

While all housing bonds are backed by the same U.S. guarantee, quite frequently bonds issued by smaller communities have sold at a lower price for a higher yield than those issued by "name" communities. Earlier this year, housing bonds issued by the bigger cities (e.g., Philadelphia, Chicago, etc.) sold at a full point premium over par while those of smaller communities sold around par.

* * * * *

The Stock Market Is Still Too High - is the current advice frequently given investor. He is advised to keep funds for investment in cash so that he will be able to invest at a later date at a lower cost. While the advice may be sound for the trader who seeks to take advantage of market fluctuations, it has questionable value for the investor who invests for the long term. Periodic investment over the long term is a form of "dollar averaging." Past statistics indicate that dollar-averaging furnishes considerable protection against market fluctuations. Over the long run, it promises the average individual investment at a lower cost than attempts to guess which way the market is going by postponing purchases when the market is "high" and making purchases only when it is "low."

The magazine "Exchange," official publication of the New York Stock Exchange, makes another point as regards "high" or "low" status of the present stock market. While various stock market indices are still quite high, 1 out of every 4 stocks listed on the New York Stock Exchange is selling at a price lower than it did in 1946. Some of those stocks represent ownership in sound companies with consistent dividend-paying records. Judging the stock market by some preconceived standard of its general level is misleading. If the particular stocks an investor is considering seem to represent good value in light of current and potential earnings, delay in purchasing because some stock market average indicates the market is too high can result in failure to make a highly rewarding investment.

Inflation Is A Continuing Problem - warns the Cleveland Trust Company. Spiraling inflation generated by World War II has given way to a gradual advance in recent years. The creeping variety of inflation may be hardly noticeable at any given time but over a decade, a 2% inflationary rate compounds to 22%. In making long-term investment, the investor must consider impact of inflation. Investment for the long term in fixed-income securities such as bonds or preferred stocks can result in loss of investment capital if inflation continues. For instance, the value of U.S. Treasury $2\frac{1}{2}\%$ bonds of 1967-1972 declined 38% in value over the last ten years.

How much inflation protection have other securities offered over the last decade? One investment advisory house gave this breakdown covering a representative listing of: preferred stocks (35% decline in value); public utility stocks (83% appreciation in value); railroad stocks (99% appreciation in value); and industrial common stocks (220% appreciation in value).

* * * * *

Estate Taxes Due On A Husband's Death - can be reduced by the marital deduction for property left a surviving spouse. The marital deduction thus allows more property to be left to the family, free of death taxes. Property left in trust for a wife will qualify for the marital deduction where she is to get all the trust income for life and has either (1) the right to dispose of trust corpus by will on her death or (2) an unlimited power to invade the trust during life. However, care must be taken to make certain that the wife's power either at death or during life over trust corpus is not limited by state law.

A husband left his residuary estate in trust, all income to his wife for life with remainder to his children. The wife was not given the right to dispose of trust corpus by will at her death. However, she was given the right during her life to use any of the trust corpus "for her maintenance, support, and comfort in her discretion." Upon demand, the trustee was required to pay over to her and she was not to be "accountable or chargeable for the use or disposal of such corpus." The husband thought that he had given his wife an unlimited power to invade the trust during her life. While the wife's lifetime power over trust corpus was not specifically designated as an unlimited power, it did not appear to be limited in any way. However, a court held that the wife's "unlimited" power to invade trust corpus was, in fact, somewhat limited.

The husband was a resident of Virginia at the time of his death. Under Virginia law, there is a presumption against disinheritance of heirs. In creating the testamentary trust, the husband was thinking of both his wife and his children. Interpreting Virginia law, the court held that the wife had a limited power to invade trust corpus during her life. As a result, the husband's estate didn't benefit from the marital deduction. Taxes on his estate were increased and the amount going to his family was reduced.

College Costs Keep Going Up - In saving for your child's education, the amount needed continues to increase. That warning comes from the U. S. Office of Education.

Figures in parentheses indicate new yearly tuition rates for private educational institutions which recently increased their annual fees: Columbia ($1,450), Northwestern ($1,245), Oberlin ($1,150), Yale ($1,550), and Tulane ($990). If your child will attend your State university, tuition fees will not be as high, but they also are being increased. Figures in parentheses indicate new yearly tuition rates: Colorado ($222), Maine ($400), North Carolina ($250), and Ohio State ($300). Board and lodging will lift costs by an additional $1,000 or more.

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REFERENCES: 1. R. J. SCHNITZER, E. GRUNBERG, W. F. DELORENZO AND R. E. BAGDON, ANTIBIOTICS & CHEMOTHER., 9:267, 1959. 2. R. C. V. ROBINSON, ANN. NEW YORK ACAD. SC., 82:(ART. 1), 144, 1959. 3. E. EDELSON, E. GRUNBERG, A. D. CALABRESE AND T. V. MORTON, IBID., P. 124. 4. P. L. WILLIAMS, IBID., P. 135. 5. F. T. BECKER AND J. L. TUURA, IBID., P. 131. 6. S. M. BLUEFARB, IBID., P. 119.

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THE MEDICAL *Bookman*

► CLINICAL MANAGEMENT OF BEHAVIOR DISORDERS IN CHILDREN

By Harry Bakwin, M.D., Professor of Clinical Pediatrics, and Ruth Morris Bakwin, M.D., Associate Professor of Clinical Pediatrics, New York University School of Medicine, New York. Ed. 2. 597 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $11.00.

Like the first edition, this text successfully fulfills the purpose for which it was written. That purpose is to stress the importance of psychologic disturbances in childhood and to be of help to those physicians whose practices are primarily concerned with the care of children. An extremely comprehensive work, it is divided into 12 major categories, including growth and development, care of the physically ill and handicapped child, etiologic factors in behavior disorders of children, organic disturbances with a large psychic component in children, and antisocial behavior. The authors have culled from the vast literature of child psychiatry the well-documented observations which have been found helpful in understanding and treating healthy as well as problem children. They have been very successful in selecting the most current and reputable articles and present an excellent bibliography at the end of each discussion.

This book is aimed primarily at pediatricians and will be most helpful to that particular group of physicians. Actually, it is a textbook of child psychiatry, although the authors seem to be particularly careful to avoid this label. It is however excellently written and organized, and will certainly be of value to all who work with children, particularly to those who are interested in the psychologic aspects of children.

E. M. L.

► DRUGS OF CHOICE (1960-1961)

Edited by Walter Modell, M.D., Director, Clinical Pharmacology, Cornell University Medical College, New York, with 47 contributors. 958 pages. 1960, The C. V. Mosby Company, St. Louis. $13.50.

As stated in the 1958-1959 edition, the objective of this volume is ". . . to provide the American physician with a comprehensive source of clear, concise, authoritative and practical answers to the continually recurring question of which drug in a rapidly changing scene is, at the critical moment, the drug of choice for an actual therapeutic problem." A survey of the text indicates an emphasis on principles of usage for the recommended drugs.

Forty-two of the 47 contributors represent internal medicine and appropriate medical and surgical specialties; five are pharmacologists. Each author has expressed his opinions of the drugs in current usage in his field of interest, with a minimum of controversial discussion.

Eight new chapters have been added. Two chapters on general principles are followed by 40 chapters devoted to agents of choice within a specialty or area of medical interest. A general subject index follows a drug index in which drugs are listed alphabetically by their generic and proprietary names.

F. T. M.

(Continued on page A-154)

she calls it "nervous indigestion"

diagnosis: a wrought-up patient with a functional gastro-intestinal disorder compounded by inadequate digestion. **treatment:** reassurance first, then medication to relieve the gastric symptoms, calm the emotions, and enhance the digestive process. **prescription:** new Donnazyme—providing the multiple actions of widely accepted Donnatal® and Entozyme®—two tablets t.i.d., or as necessary.

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► ANATOMY
A Regional Study of Human Structure

By Ernest Gardner, M.D. and Ronan O'Rahilly, M.D., Wayne State University College of Medicine, Detroit, and Donald J. Gray, Ph.D., Stanford University School of Medicine, San Francisco. 999 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $15.00.

Presumably, no one, except perhaps first-year medical students, ever reads an entire textbook of anatomy. However, once the reader has examined this excellent book, he probably will be induced to peruse those topics in which he is interested. From this point, it should be easy for him to come to rely on this text as a means of refreshing his knowledge of anatomic details. The book also will serve as a source for references to recent anatomic literature and as an introduction to new information.

This is another of the new texts designed especially for the current courses in gross anatomy offered to medical and dental students; it is a noteworthy addition to the texts already available. Its regional approach, obviously best suited to the study of anatomy, is only one of the features to recommend it. There is constant emphasis on the functional importance and clinical aspects of the anatomy presented. Where the subject matter is thought to warrant it, as in the case of both the thorax and the abdomen, there are special chapters on the surface anatomy and physical examination and on the radiologic aspects of the anatomy of the region.

The text is replete with footnotes that give references to points cited, explanations of terms, and sometimes information concerning the incidence of and variations in the particular details described. Many chapters are also followed by a short list of more general references. The use of small type for the footnotes, references and a fairly large amount of textual material allows a great deal of information to be included in the pages of this book.

The illustrations, except for the numerous roentgenograms, are line drawings, varying from highly schematic ones useful in teaching to accurate representations of the anatomic points to be illustrated. The roentgenograms apparently have been painstakingly chosen for their clarity, and are probably the best series yet to appear in an anatomic text.

W. H. H.

► PRACTICAL PROCTOLOGY

By Louis A. Buie, Sr., M.D., Emeritus Member, Section of Proctology, Mayo Clinic, Rochester, Minnesota. Ed. 2. 737 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $22.50.

Dr. Buie was for many years in charge of the Section of Proctology at the Mayo Clinic, and his wealth of experience is reflected in the revision of this book, first published in 1937.

The section on examination is exhaustive and laudably devotes considerable attention to the psychology of handling the patient, a matter not to be overlooked. The pathogenesis of anorectal disease is discussed clearly and in detail, and basic embryology and anatomy of the pelvis are admirably described. Anorectal pathology and treatment are covered thoroughly. The chapter on ulcerative colitis is particularly detailed, especially in regard to pathogenesis and the sequence of pathologic events; it should be especially valuable even for the experienced proctologist.

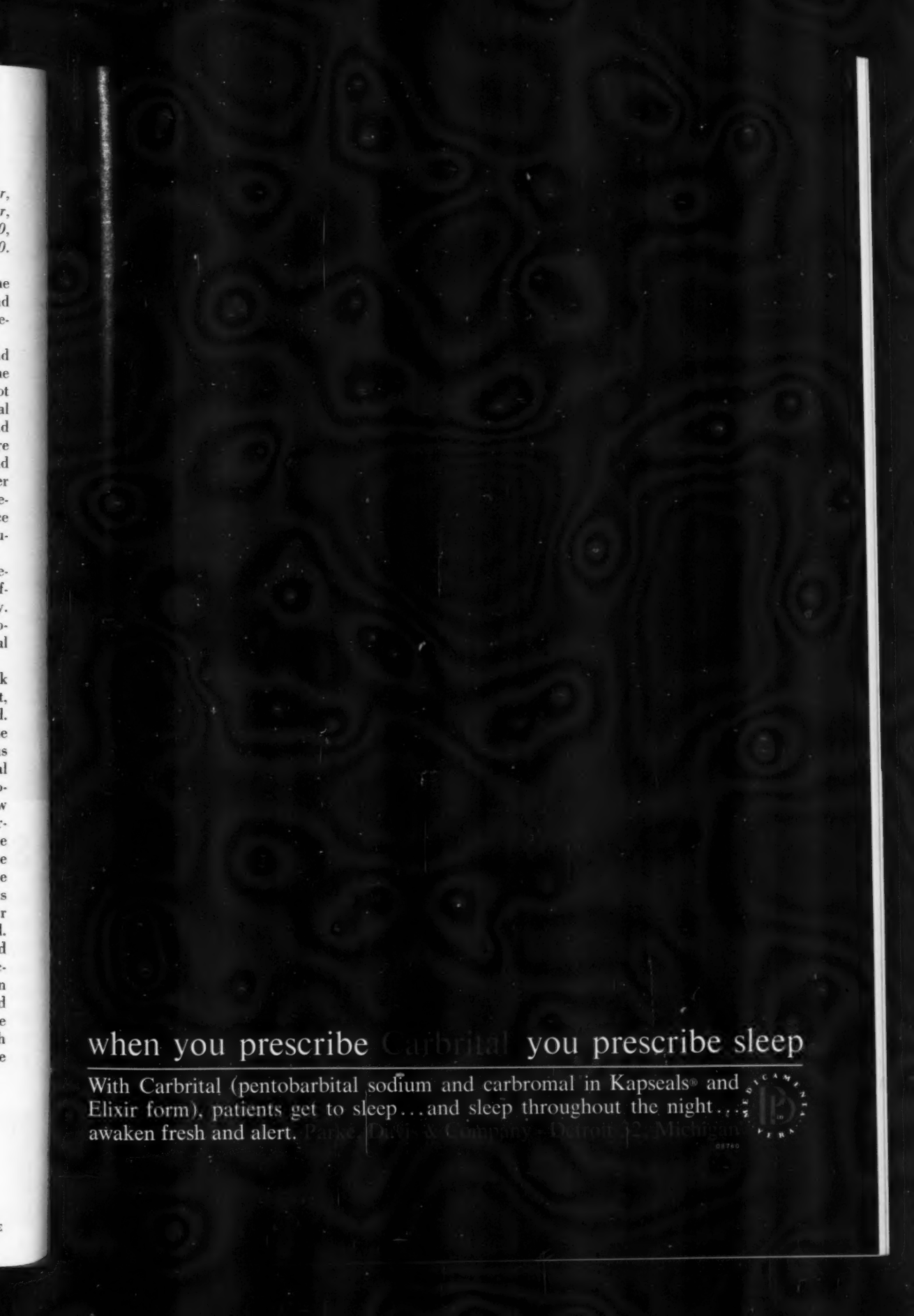
Although anorectal surgical technic is well described and illustrated, no descriptions are offered of colonic operations involving laparotomy. I feel that undue emphasis is given to such procedures as fulguration and irradiation of rectal cancer.

In spite of the general excellence of the book as a treatise on anorectal disease and treatment, a few adverse criticisms could be mentioned. Among these is the recommendation for the use of No. 1 catgut in hemorrhoidectomy as well as the postoperative use of rubber drains in the anal canal. Classification of rectal prolapse and procidentia adheres to the older terminology (now largely abandoned by colonic and rectal surgeons), which is more confusing than the simple categories of prolapse and procidentia used more generally today. The complication of massive hemorrhage in diverticular disease, in spite of its importance, is barely mentioned, and neither coccygodynia nor proctalgia fugax is discussed.

Even with these minor defects, the book should be eminently instructive for the general practitioner and the medical student; the section on pathogenesis of ulcerative colitis should be read by all who are interested in colonic disease. The author has a superb command of the English language and his editorial skill can hardly be improved.

S. T. R.

(Continued on page A-156)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► NEUROLOGY

By Roy R. Grinker, M.D., Director, Institute for Psychosomatic and Psychiatric Research and Training, Chicago, Paul C. Bucy, M.D., Professor of Surgery, Northwestern University Medical School, Chicago, and Adolph L. Sahs, M.D., Professor, Department of Neurology, State University of Iowa College of Medicine, Iowa City. Ed. 5. 1,386 pages with 445 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $24.50.

Ten years have elapsed since the fourth edition of this well-known textbook of neurology was published. The fifth edition reflects the rapid progress in this field by an increase of 20 per cent in the number of pages and by the addition of a third author. The authors also acknowledge the assistance of a group of distinguished specialists who were consulted in their various fields.

The text shows evidence of extensive revision to bring it up to date. The opening chapter, dealing with the neurologic examination, has been expanded from 68 to 100 pages. The portion of this chapter concerning roentgenographic examination now includes a discussion of angiography, and the quality of the reproductions of roentgenograms is far superior to that in the previous edition. The section on electroencephalography has been rewritten completely to give a brief but well-balanced appraisal of the field, including such recent topics as the controversial 14-per-second and six-per-second positive spikes.

For the first time a chapter has been devoted to neurochemistry and metabolic disorders of the nervous system. This subject is still in its infancy, so the concept of "neurochemical lesions" is stimulating more because of its promise of knowledge to come than because of its present usefulness.

The chapter dealing with infectious diseases of the nervous system is excellent. The great strides made in chemotherapy during the interval between the last two editions have resulted in a far brighter outlook for many patients with inflammatory processes of the nervous system. Although 25 pages are devoted to the discussion of neurosyphilis, this disease is fast disappearing, and it is possible that some younger physicians using this volume will never have the opportunity to see the various forms of neurosyphilis which are described.

Encyclopedic in scope, this volume is also well abreast of the recent developments in the broad field of neurology. Its depth of coverage naturally is not as great as that of the multivolume opera for the neurologic specialist; however, it is an ideal book to broaden the knowledge of interns and residents, to refresh and extend the information of physicians who encounter neurologic problems in their practice, and to serve as a ready reference book for the neurologist.

D. D.

► CHRISTOPHER'S MINOR SURGERY

Edited by Alton Ochsner, M.D., Professor of Clinical Surgery, Tulane University School of Medicine, New Orleans, and Michael E. DeBakey, M.D., Professor of Surgery, Baylor University College of Medicine, Houston, with 24 contributors. Ed. 8. 539 pages with 347 illustrations. 1959, W. B. Saunders Company, Philadelphia and London. $10.50.

As in previous editions of this book, emphasis in the present volume is on diagnosis and treatment of surgical conditions that can be managed at home, at the office, or in the hospital treatment room. Three valuable new chapters have been added on injuries of the hand, diseases of the breast, and physical treatment in minor surgery.

In some sections, the original intent of this book is not followed, in that diseases and diagnostic procedures that can be handled only by hospitalizing the patient are presented; however, the book is chiefly a treatise on office surgery. Of particular value are the sections on mechanical injuries, burns, musculoskeletal injuries and injuries of the hand.

The section on anesthesia is rather general for the most part, but the portions devoted to nerve blocks and to resuscitation are well illustrated and practical. Other discussions include such fundamental aspects as equipment in minor surgery, dressings, and bandages. An instructive chapter on the conduct of surgical residents is included.

The discussions are brief and concise and emphasize diagnosis and treatment. Most of the contributors take the viewpoint that no surgical procedure is to be regarded lightly and that proper management in the office requires organization, adequate equipment, planning and preparing for emergencies.

Y. S.

(Continued on page A-160)

new compound from Mead Johnson Research

tacaryl T.M.

METHDILAZINE HYDROCHLORIDE, MEAD JOHNSON

for prompt, prolonged relief of allergic symptoms through inherently sustained action at the cellular level...with b.i.d. dosage

inherently sustained action

Tacaryl possesses inherent long-acting properties. After rapid disappearance from the blood serum, Tacaryl is bound to the tissues. This protective affinity for tissue provides a notably sustained effect which does not depend upon the use of artificial, long-acting construction. The sustained action is an inherent property of the molecule and lasts for periods up to 12 hours.

rapid absorption—rapid relief

Tacaryl is absorbed quickly to provide rapid relief of symptoms. This action is due to the rapid transport of Tacaryl from the blood stream to the tissues.

low toxicity—minimal side effects

In studies to date,[1] side effects were minimal; only in a small percentage of cases was mild drowsiness observed. Tolerance was not reported even after long usage. No cumulative effect has been observed.

clinically proved in a wide range of allergic and pruritic conditions

In a study of 459 patients[1] Tacaryl provided effective symptomatic relief in a wide variety of conditions including allergic rhinitis, pruritus, various skin disorders, allergic bronchial asthma, pruritus of chickenpox and allergic conjunctivitis. In some cases, the relief of itching bordered on the dramatic.[2] In a double-blind clinical evaluation[3] of various antihistaminic agents in hay fever, Tacaryl provided benefits in all patients with moderate to severe symptoms.

dosage: Adults: *Tablets*—One tablet (8 mg.) twice daily. *Syrup*—Two 5 cc. teaspoonfuls (8 mg.) twice daily. Children: *Tablets*—One-half tablet (4 mg.) twice daily. *Syrup*—One 5 cc. teaspoonful (4 mg.) twice daily.

In some patients it may be desirable to adjust the dosage to meet individual requirements.

supplied: Scored tablets, 8 mg., bottles of 100. Syrup, 4 mg. per 5 cc. tsp., 16 oz. bottles.

references: (1) Clinical Research Division, Mead Johnson & Company. (2) Howell, C. M., Jr.: Evaluation of Methdilazine as an Antipruritic Agent, North Carolina M. J. *21* (May) 1960 (in press). (3) Wahner, H. W., and Peters, C. A.: An Evaluation of Some Newer Antihistaminic Drugs Against Pollinosis, Proc. Staff Meet. Mayo Clin. *35*:161-169 (March 30) 1960.

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► METABOLIC CARE OF THE SURGICAL PATIENT

By Francis D. Moore, M.D., Moseley Professor of Surgery, Harvard Medical School, Boston. 1,011 pages with 143 illustrations. 1959, W. B. Saunders Company, Philadelphia and London. $20.00.

As the title implies, this book deals with the metabolic care of the patient both before and after surgical procedures. The book is divided into six parts, each of which consists of 6 to 10 chapters. Following a discussion of the normal person and his metabolism and endocrinologic status, the author considers convalescence from surgery and the variation in response in the very young and very old patient. He next discusses the effects of loss of blood and plasma and those of hypervolemia, transfusion, electrolytic abnormalities and nutrition and starvation. Effects of visceral disease on surgical patients and the metabolic effects of fractures, traumatic wounds and burns also are covered.

The text is well written, generously illustrated, and has an extensive bibliography. There are 32 case reports which illustrate general principles in the metabolic management of patients. This book will be invaluable to all surgeons because, as the author states in his introduction, the surgeon must be aware of postoperative metabolic changes in order to give his patient the best possible care. It also will be of value to internists, since they are consulted so often to see patients who have postoperative complications.

R. V. R.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers are reviewed more extensively.

First Aid; Diagnosis and Management. By Warren H. Cole, M.D., Professor and Head of the Department of Surgery, University of Illinois College of Medicine, Chicago, and Charles B. Puestow, M.D., Chief, Surgical Service, Veterans Administration Hospital, Hines, Illinois, with 16 contributors. Ed. 5. 420 pages, illustrated. 1960, Appleton-Century-Crofts, Inc., New York. $6.25.

Myocardosis. By Ferdinand Wuhrmann, M.D., Chief, Medical Service, Cantonal Hospital of Winterthur, and Serge Niggli, M.D., Resident, Medical Service, Universitat Zürich Medizinische Fakultat, Zurich, Switzerland. Translated by Harvey T. Adelson, M.D. 218 pages with 61 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $10.50.

Medical, Surgical and Gynecological Complications of Pregnancy. By the staff of Mount Sinai Hospital, New York. Edited by Alan F. Guttmacher, M.D., Obstetrician and Gynecologist-in-Chief, and Joseph J. Rovinsky, M.D., Assistant Attending Obstetrician and Gynecologist, Mount Sinai Hospital. 619 pages, illustrated. 1960, The Williams & Wilkins Company, Baltimore. $16.50.

Wolff's Diseases of the Eye. Revised by Redmond J. H. Smith, F.R.C.S., Consultant Ophthalmic Surgeon, St. Mary's Hospital, London, England. Ed. 5. 226 pages with 150 illustrations, five color plates. 1960, Charles C Thomas, Springfield, Illinois. $9.50.

Clinical Endocrinology. Edited by Edwin B. Astwood, M.D., Professor of Medicine, Tufts University School of Medicine, Boston, with 82 contributors. No. 1. 724 pages, illustrated. 1960, Grune & Stratton, Inc., New York and London. $18.75.

Surgery of Repair as Applied to Hand Injuries. By B. K. Rank, F.R.C.S., Honorary Plastic Surgeon, Royal Melbourne Hospital, and A. R. Wakefield, F.R.C.S., Plastic Surgeon, Royal Children's Hospital, Melbourne, Australia. Ed. 2. 284 pages with 219 illustrations. 1960, The Williams & Wilkins Company, Baltimore. $9.00.

Diseases of the Nervous System in Infancy, Childhood and Adolescence. By Frank R. Ford, M.D., The Johns Hopkins Hospital, Baltimore. Ed. 4. 1,548 pages with 215 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $29.50.

The Haemolytic Anaemias; Congenital and Acquired. Part 1. The Congenital Anaemias. By J. V. Dacie, M.D., Professor of Haematology, University of London Faculty of Medicine, London, England. Ed. 2. 339 pages with 118 illustrations. 1960, Grune & Stratton, Inc., New York and London. $7.00.

An Introduction to Gynecological Exfoliative Cytology. By Winifred Liu, M.D., Cytologist, Youngstown Hospital Association, Youngstown. 127 pages with 40 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $6.00.

Pediatric Anesthesiology. By M. Digby Leigh, M.D., Associate Professor of Surgery (Anesthesia), and M. Kathleen Belton, M.D., Assistant Professor of Surgery (Anesthesia), University of Southern California School of Medicine, Los Angeles. Ed. 2. 461 pages with 203 illustrations. 1960, The Macmillan Company, New York. $12.00.

Radiologic Examination of the Small Intestine. By Ross Golden, M.D., Visiting Professor of Radiology, University of California at Los Angeles School of Medicine, Los Angeles. Ed. 2. 560 pages with 176 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $28.50.

Communicable and Infectious Diseases; Diagnosis, Prevention, Treatment. By Franklin H. Top, M.D., Professor and Head, Department of Hygiene and Preventive Medicine, State University of Iowa, Iowa City, with 21 collaborators. Ed. 4. 812 pages with 122 illustrations and 15 color plates. 1960, The C. V. Mosby Company, St. Louis. $20.00.

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DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

May 1—To luncheon came Charles Wilinsky and Lily and Justin and all the family. In the evening to the Drake Hotel where some 200 assembled to launch the Mental Health Center of America which is in Denver. Judge Kerner spoke, and here also were Otto Bettag, Julius Masserman, William Long, and representatives of the Oil, Chemical and Atomic Workers Union. Dr. Alan Kraft told of the work of the institute.

May 2—In the afternoon to sit with Sol DeLee, M. Edward Davis and Ralph Creer, designing some motion pictures of obstetrics. Thereafter to a reception for the Consul General of Israel on the tenth anniversary of the founding of that small nation. In the evening to attend a dinner with 1800 people where Otto Bettag presided and Maxwell Jones of England told of community rehabilitation of the mentally disturbed. He told of the Maudsley Colony in England where after their discharge some 60 per cent of the patients were able to remain outside. He said it is easy to change the culture of a hospital but not so easy in the surrounding community, and urged particularly the education of the public regarding mental illness. Finally he stated that the general practitioner is the real psychiatrist for the mass of the people.

May 3—To the dentist for a final look before going abroad. At noon to confer on the Salute to Medical Research of the City of Hope and then in the afternoon came R. T. Hewitt of the Royal Society of Medicine.

May 4—By the early plane to New York, reading en route "The Chapman Report" by Irving Wallace, a most exciting concept—namely, what happens to a small town where all the women participate in making a Kinsey report. At once to meet with John Beckley at Warwick & Legler on a program for health education. Then to Vincent Nelson at Thos. Cook for details of travel abroad and after that with Elmer Bobst and Len Scheele to confer with a high government official on plans for the care of the aged. In the evening by plane to Chicago.

May 5—Early came John Bach with a plan for a periodical to be devoted to the many addresses made before medical organizations. Then met with Bob Dachman to consider the development of the Chicago Medical School where he is to become an official. In the afternoon came Chaplain Wennerstrom of the Billings Hospital with the program for a new organization concerned with the costs of mortuary services and the problems of securing postmortems and anatomic material. For dinner with Louis Mann where were also the Kirsners, the Altschulers and Maurice and Joel Goldblatt.

May 6—Early to see Don McNeill and to participate in his program before some 700 high-school seniors. So old Pepys answered questions about sleep, diet, exercise and medicine. Thereafter came Armand Partipilo with his novel which continues to develop romantically. At noon came Mr. J. Douglas Knox, who is developing a great plan for improving medical communications through the National Institutes of Health. Finally at my scrivening.

May 8—Greeted Mistress Pepys with best wishes for Mother's Day which is a *fiesta* honoring the florists. In the afternoon all the family to greet Grandma, now approaching 92 years of age, and then to Ravisloe where some 20 of us dined and discussed and said farewells, for soon the great trip abroad begins.

May 9—By the 6:30 A.M. plane to Louisville and greeted at the airport by Mistresses Zollinger and Nancy Hall who arranged matters for the tuberculosis association. Next interviews and films for the press and at noon to speak to some hundreds in the Kentucky Hotel, formerly Brown's, on the countdown in tuberculosis. Here Irvin Abell, Jr., president of the Kentucky State Medical Association, spoke most reminiscently of his distinguished father. Dr. Davidson was chairman. Then at 5:00 P.M. off to New York.

May 10—To the Warner-Lambert stockholders' meeting. At noon to luncheon with Bill White, Max Geffen, Irvine Page, Silver and Harold Diehl at the RCA Club to consider more ideas for *Medical World News*. Next Tom Rivers with Terese and then Elmer Bobst, the William Lasdons, Sorokos, Kellys, Runyons and Mademoiselle Said from Lebanon for cocktails. So with the Runyons, Sorokos, Herbert Mayes and Hewitt of London to dine at The Four Seasons, and say more farewells.

(Continued on page A-176)

important new therapy in Peptic Ulcer

cessation of all symptoms and complete healing in 70 out of 78 cases as reported in Postgraduate Medicine (Oct.) 1959

"... chymotrypsin offers a new approach to the treatment of peptic ulcer."

In 54 cases, most of them hospitalized, in which chymotrypsin (Chymar) was used in conjunction with other agents "All of the symptoms disappeared and *complete healing of* the ulcer occurred in 49 (90.7 per cent) of the 54 cases . . . " Average time for cessation of symptoms . . . 6 days; for complete healing . . 36 days; average follow-up period . . . 12 months. *In 24 cases* in which Chymar was used alone, "Cessation of all symptoms and *complete healing occurred in 21 (87.5 per cent)* of the 24 cases . . ." Average time for cessation of symptoms . . . 5.8 days; for complete healing . . . 24 days; average follow-up period . . . 25.5 months.

Conclusions: "Because of the excellent results obtained in 78 cases of peptic ulcer . . . I strongly recommend its use as a most valuable adjunct in the treatment of this disease."*

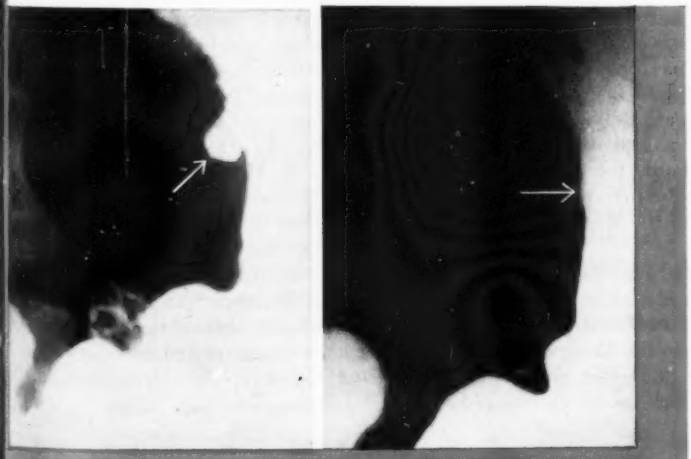
*Mozan, A. A.: Postgraduate Med. 26:542, 1959

the superior anti-inflammatory enzyme

Chymar®

chymotrypsin *Buccal/Aqueous/Oil*

controls inflammation, swelling and pain



Pretreatment roentgenogram made on January 26, 1957 shows a large niche on the upper third of the lesser curvature.

Roentgenogram made on February 23, 1957 shows only a slight indentation on the lesser curvature.

CHYMAR Buccal—Crystallized chymotrypsin in a tablet formulated for buccal absorption. Bottles of 24 tablets. Enzymatic activity, 10,000 Armour Units per tablet.

CHYMAR Aqueous—Solution of crystallized chymotrypsin in sodium chloride injection for intramuscular use. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

CHYMAR—Suspension of crystallized chymotrypsin in oil for intramuscular injection. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

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May 11—By Pan American jet to London in six hours' flying time most comfortably and spent the night at Claridge's. En route read all the magazines and also "The Lincoln Lords" by Hawley, which includes an exciting story on the launching of a baby food. Stanley Henwood came for late supper and discussed the coming congresses on congenital malformations and poliomyelitis.

May 12—By the BEA Comet to Rome in two hours. At the airport the Marino-Zucos, Pizzetti and Romola Vicchi. Then to dine on the Hassler roof.

May 13—Early awake and to the Information Service for news and the magazines. On my new Olivetti writing letters, book reviews and editorials for various publications. At noon to luncheon at Doney's where saw Grace from Brooklyn and then to the Excelsior where Horace Turner just arrived with Edelman from Chicago, ready to establish the registration for the International College of Surgeons. Then to the Hassler roof where Mistress Pepys had luncheon with Mrs. Alberto Del Torto, as wholly charming as always.

May 14—The crowds begin to assemble for the meeting of the International College of Surgeons. In the lobby of the Hassler met Alex Brunschwig and thereafter walked to the Excelsior Hotel and sat with the officers and delegates who chose Lionel Appleby of Canada as president-elect, Horace Turner as secretary-general, and Arnold Jackson as assistant secretary-general. Here were Compere just arrived from Munich and also saw Gus Daro of Chicago, but many sent proxies. New York was chosen as the place of meeting in 1962.

In the evening to the Open Gate Club where Dr. Piedro Valdoni and his gracious lady entertained well-nigh 100 guests at a beautiful dinner with dancing and entertainment. This was a great occasion with representatives of 25 or 30 nations.

May 15—Early awake and went to the great Palace of Congresses where some 2000 visitors attended the opening session. Here Dogliotti spoke on extracorporeal circulation, saying that he had first practiced this procedure in 1951 and saw for it great uses not only in surgery but also in internal medicine. Valdoni and Bendandi spoke and also Meyerding and Turner. Old Pepys sat on the dais next to the great Böhler of Vienna who many years ago came to a meeting of the Minnesota Medical Association in Duluth and had a photograph taken with Dr. Will Mayo and old Pepys. In the afternoon came the Del Tortos and Douglas Wist with his new bride Mary, and we had a fine luncheon and talked for some hours of experiences of the American troops in Germany. In the evening to the thermal baths of Diocletian which are just beyond the Grand Hotel and which house a great museum of sculptures of early days. In the crowd of visitors old Pepys greeted Branco Ribeiro of São Paulo, Taiana of Buenos Aires, Dr. Huding of the Netherlands, Drs. Sideman, Rolnick and Parker of Chicago, and many surgeons from all around the world. Thereafter with Pietrogrande, Romola Vicchi and the Marino-Zucos to dine.

May 16—Early to work and received a great package of manuscripts to be edited. In the afternoon to the Congress and heard Domagk predict the end of surgery for cancer and describe a new cytostatic drug. Then young Frugoni showed some 90 per cent "cures" in patients with arteriovenous aneurysms on whom he had operated. Next Professor Cattaneo of Rome talked about cancer of the cervix. Professor Marino-Zuco then told of his treatment of fractures of the femur, having used of late a development from America involving the employment of a polyurethane plastic which can be put into the bone and acts like reinforced concrete to hold the parts in position. To dinner came Professors Chain, Frontali, Gozzano and Marino-Zuco with the ladies. Professor Chain doubts that any antibiotic will ever control cancer, because of the varying nature of the cancer cells.

May 17—Early awake and after some hours of scrivening to the Instituto Superiore di Sanita to talk with Professor Marotta, who had just completed hosting a congress on fermentation and who departs shortly for Russia for another. Then an hour with Professor Chain, who told me of great progress with a new penicillin and also a technic for preparing lysergic acid in quantity and the particular interest in brain chemistry. Thereafter to our embassy for an hour with John Brown, formerly of Hamilton College, who heads the American information service which is doing notably to show Italians that Americans also have an interest in cultural activities. At lunch with Madame Brunschwig and reminisced of the older days when they lived at Woodlawn near the University. In the evening to a great reception at the home of Professor Carlo Marino-Zuco where among the guests were the Comperes and Sidemans from Chicago, the Thompsons

(Continued on page A-178)

The Aged

–and a natural way to meet their special nutrition needs with fresh-flavor, economical Carnation Instant.

Finicky appetites, dental problems, food costs—one or more often play a part in contributing to poor diet for the elderly.

A pleasant *natural* way to help improve their nutritional status is the excellent new food—*new Carnation Instant Nonfat Dry Milk mixed 25% over-strength.*

One-third cup extra crystals per liquid quart when mixing provides 25% more calcium, protein, and B-vitamins than ordinary nonfat milk. Because your patients can add this additional amount, they get *needed* nutrients *—without* excessive calories. And its richer, more delicious flavor mixed over-strength is a *natural* way to *extra* nutrition they'll enjoy. Costs them only 10¢ a quart.

ANOTHER QUALITY PRODUCT OF CARNATION COMPANY. LOS ANGELES 36. CALIFORNIA

from Medford, Oregon, Cantwell from New York, and Professors Valdoni, Dogliotti, Camara and Frontali, the Del Tortos, Conforty from Sofia in Bulgaria, Bulgari, most famous jeweler, and all the ladies.

May 18—At noon to Pasietto's with Madame Fontana, a world-renowned designer, and with her Madame Picelli and her husband who is assistant secretary of state. We talked of a new organization designed to aid crippled children in Italy where rehabilitation for the mass is in its infancy. In the afternoon came James Cauverien and Els to tell of work now going on for the International Neurological Association, which will meet in Rome in 1961. In the evening with the Marino-Zucos to a great dinner and ball. Here Professor Valdoni presided and received the honorary fellowship of the College. Medals were given to the retiring president, Henry Meyerding, and recognition to representatives of each of the leading nations. Old Pepys sat between Madame Boshamer of Germany and Madame Huding of the Netherlands and we talked about the trip of James Boswell into Holland and of the great changes in Germany since the end of the war. Here greeted Dr. Leon Edelstein of the California State Board of Examiners and Claude Hunt with his dear lady from Kansas City, and many friends from many nations. This social occasion in itself showed the great merit of international meetings, apparently doing far more for the cause of peace than is ever developed in such gatherings as the Summit in Paris.

May 19—With Madame Gozzano to visit the beautiful sanatorium near the Pallazo del Congressi on the Cristoforo Colombo road which she and the professor developed for mildly ill mental patients. To luncheon came Professor and Madame Caronia and also Romola Vicchi. Then with Dr. Carlo Marino-Zuco and Elena to the airport where *Signore* Marino who directs it made all easy for us, but old Pepys had mislaid his own *signora's* passport and there was great consternation until ultimately it was found in a book by Schilling called "The Fear Makers." At the airport met Dr. and Mrs. Claude Hunt of Kansas City and also Mike Leventhal of the Stein-Leventhal syndrome, on the way to talk about it in Israel. So arrived in Israel and met by Dr. Solowiejick, who represented the College of Surgeons. Then a three hour drive to the Hotel Dolphin beyond Haifa on the Mediterranean Sea.

May 20—Early awake and drove to Nazareth and Galilee and around Mount Carmel. In Haifa with Dr. Izkovitch visiting the gorgeous physicians' hall which he led in building, housing also a library, kitchen and dining room and all the necessities for a physicians' organization. The hall has perfect acoustics and provisions for movie projection. Haifa now has 180,000 people with 800 physicians, new buildings, a modern theater, fine restaurants and bookstores. So then driving on to the Ramat Aviv in Tel Aviv. In the evening to a beautiful reception at the fine home of Dr. Max Marcus, leading surgeon, where came many old friends not only from this area but also Zimmerman and Parker from Chicago, Gordon from Detroit, Fairer from San Francisco, Horace Ayres from New York, Brailsford from England, and many, many more. Here met again Neumann, who heads the physicians of the Histadrut and who is coming for three months on an International Labor Organization fellowship to study industrial surgery in the United States. Here also Dr. Horel, who conducts the great private Assuta hospital with 150 beds in Tel Aviv.

May 21—This day driving to Beersheba on the upper edge of the Negeb desert. A fine hotel set up by the HIAS provides excellent services. A new hospital, finished in January 1960, is ultramodern yet fully adapted to the needs of a tropical area. So home by way of Rehovot for a look at the Weizmann Institute. In the evening to a session at the doctors' building, greeting again Bernhard Zondek, M. Sherman, N. Sinai, J. Asherman, representatives of the municipality and the ministry of health, also Meyshan, Berlin, and from America, H. Kessler. Zondek told how sound, both supersonic and a bell rung for one minute at 10 minute intervals for 24 hours, inhibits ovulation, decreases fertility, interferes with implantation of the ovum, and greatly reduces the yield of fetuses in 1000 rats tested with controls and also in 48 rabbits.

May 22—Early on a two hour drive to Jerusalem from Tel Aviv seeing many historical Arabic and Israeli villages. Then to see the new Hebrew University, most modern in construction with a great library all air-conditioned and a great reading room named in honor of my friend Katzen from Chicago. The chapel is terrific in its stark simplicity. The lecture halls are unique in quality of acoustics and arrangements. Next with Aaron Brand, chairman of the medical society,

(Continued on page A-180)

RONCOVITE®-MF
IS RAPIDLY BECOMING THE DRUG OF CHOICE IN ANTI-ANEMIA THERAPY...

because...

Cobalt is the only known clinically proved therapeutic agent which enhances the formation of erythropoietin, the hormone which regulates erythropoiesis in the body.

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Roncovite through the effect of Cobalt-enhanced erythropoietin improves iron utilization by activating this normal physiologic process.

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The result is a more rapid and complete hematologic response in the anemic patient . . .

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The safety of Roncovite has been demonstrated by the administration of over 365 million doses.

Please write for monograph, "The Hormone Erythropoietin." Roncovite literature also available on request.

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Cobalt chloride . . . . . 15 mg.
(Cobalt as Co. 3.7 mg.)

Ferrous sulfate, exsiccated . . . . . 100 mg.

DOSAGE: The maximum adult dose of Roncovite-MF is one tablet after each meal and at bedtime.

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to see their new building and met there Roy Grinker, who was delivering a lecture on neurologic research. Thereafter to the Brand home to meet the wife and children, then to a luncheon given by the officers of the medical organization at the King Hotel, where were Avigdori, Munter, Soriano, Brand, Ungar, Nelken, librarian who knows all the literature, and the ophthalmologist Landau. Thereafter to view the great headquarters of the rabbinate with their supreme court and a museum of rare treasures, including manuscripts which rivaled the Dead Sea scrolls on exhibit at the University. Next with Dr. Prywes, vice-president and dean of the Hadassah Hospital and the medical school, to see the construction on their new medical center. At the hospital in the center of the city with Aaron Brand and Dr. Kagan and saw a new pediatric division with a special section on rheumatic fever. This disease is still quite prevalent in Israel, although the death rate from tuberculosis is now down. For tea to the home of Drs. Hermann and Gilda Zondek, and reminisced of old times. So stopped at the King David Hotel for a chat with Roy and Mildred Grinker, then drove to Tel Aviv and met there Viola Cantor Tatum's mother, and Doris Schoen and her son, and then Starkman came with the little girl who was rehabilitated at Rusk's Institute.

May 23—Early awake and to the airport in Lydda near Tel Aviv. En route reflected on the tremendous progress visible everywhere since we were here in 1952. In Istanbul greeted by our old friend from Thos. Cook whose symptoms make a whole clinic. So to the beautiful Istanbul-Hilton.

May 24—To the Russian consulate to see about visas and they said to come back at 2 o'clock. Visited the bazaar where hundreds of enticing shops were spread over many miles. Back to the consulate at 2 and they said to come tomorrow at 10.

May 25—Early awake and to the Russian consulate for an interview with the consul to whom Mistress Pepys spoke in French and they got along well until suddenly he produced more forms to sign and said come back at 2. At 2 came back and was handed the visas for Moscow and Leningrad and great packages of tourist literature. Then met Henry Kessler and his lady and we toured the Sultan's palace to see the china and the treasures, and saw the reservoir built by Justinian I in the sixth century. At tea met Mario Cavaseppi and his brother who come from Naples.

The Medical Muse

RICHARD ARMOUR

OF AGE

Commonly, physicians, like beer, are best when they are old; and lawyers, like bread, when they are young and new.—*Thomas Fuller, seventeenth-century English clergyman.*

The lawyer who's an aging oldie,
Like bread may get all stale and moldy,
Instead, indeed, of growing yummy,
May get to be a little crumby.

The doctor, though, and let us cheer,
Improves with age, like lager beer,
Gets sharp, like Camembert or Cheddar;
Instead of getting worse, gets beddar.

So courage, aging doctor, if'n
Your joints mayhap begin to stiffen.
Remember this, from this here poet:
You're at your best, though you don't know it.

MECHANICAL FAILURE

According to Dr. Albert Stunkard of the University of Pennsylvania, obese women who overeat do so because of a failure of the brain's signal mechanism to indicate when hunger has been satisfied.—*News item.*

The woman who has grown obese
Has had, it seems, tough luck.
The signal mechanism in her brain
Is out of whack, or stuck.

The lights don't flash, the flags don't wave,
The little gong's not beaten,
So how is she, though overweight,
To know she's overeaten?

And so she stuffs herself with sweets
Until she's crammed and bloatified.
She really isn't hungry, but
She's waiting to be notified.